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An essay on the circulation as behavior

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Abstract: Most conceptual models of the organization of the cardiovascular system begin with the premise that the nervous system regulates the metabolic and nonmetabolic reflex adjustments of the circulation. These models assume that all the neurally mediated responses of the circulation are reactive, i.e., reflexes elicited by adequate stimuli. This target article suggests that the responses of the circulation are conditional in three senses. First, as Sherrington argued, reflexes are conditional in that they never operate in a vacuum but in a context together with other reflexes. Guided by functional utility, they interact rather than add. Second, as Pavlov argued, stimuli acquire meanings as a result of experience. This notion of stimulus effect plus the Sherringtonian notion of conditionality suggest that association is one of the ways stimuli eliciting cardiovascular reflexes acquire their meanings and thus their relative strengths. Finally, as Skinner and others have argued, operants are responses that act upon the environment to obtain consequences – that is, stimuli. As operants, cardiovascular responses fulfill a major biological need, functioning proactively. The cardiovascular response is an integral component of the animal's behavior regardless of whether it is an elicited reflex or the eliciting stimulus acquired its properties as a result of the genetic inheritance of the animal or through experience, or the cardiovascular response is emitted in anticipation of an environmental consequence. The main theses of this essay are: (1) behavior is an integrated set of responses and the circulation is one of the response systems comprising behavior; (2) behavior is, in part, determined by its functional significance within a context; (3) the contextual factors operative at the time of the behavior have a major role in determining which of the set of possible responses will determine the final act, that is, which behavior will be the effective response and which other behaviors will be concomitants.

Keywords: behavior; biofeedback; cardiovascular responses; circulation; conditioning; learning; motor equivalence; neural regulation of circulation; reflexes

1. Introduction

The purpose of this target article is to review what I believe is now overwhelming evidence that the responses of the circulation in awake vertebrates are conditional and are integral components of the behavior of the animal. By conditional, I mean: (1) The responses will vary as a function of the stimuli that impinge upon the animal. I wish especially to emphasize here the interactions among stimulus effects. This is conditionality, in Sherrington's sense, when he described the various ways stimuli can interact to modulate reflexes. (2) The responses will vary as a function of the associative characteristics of the environmental cues – conditionality in Pavlov's sense. (3) The responses will vary as a function of their ability to interact directly with the environment – conditionality in the operant sense. By behavior I mean the sum total of the organism's interactions with its environment. Thus, autonomically mediated and hormonally mediated responses as well as somatically mediated responses are all behaviors. As a matter of fact, an underlying principle of this essay is that, from the perspective of behavior, the distinction between, for example, somatomotor and visceral behavior is only valid in the sense that these behaviors are mediated by different anatomical and physiological structures that impose idiosyncratic constraints on their respective performances. I will limit my discussion and my argument to an analysis of the circulation.

2. Stimulus interactions

Sherrington (1973) noted and documented the fact that reflex, somatic responses to afferent stimuli were neither independent nor additive. That is, a reflex that could be elicited in an isolated system might behave much differently if it were elicited in the presence of other stimuli. For example, if the afferent root of the 7th or 8th cervical nerve of the monkey is stimulated, there is either a flexion or an extension of the elbow; if the 1st thoracic root is stimulated first, the response is an extension, but if one first stimulates the 6th cervical root, the response will be a flexion. What Sherrington (1973) noted and underscored was that only one of the two reflexes appears, and that an algebraic summation would be useless (p. 119). A large number of interactions among stimuli is possible; for example, facilitation, inhibition or irradiation to other response systems; however, what one is most likely to see, as Sherrington emphasised, is a functional act.

There has been a great deal of research on stimulus

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interaction effects on the reflexes of the circulation, but this research has been considered primarily in terms of the specific reflexes in question rather than in the broader context of a principle such as the one Sherrington proposed to characterize reflexes. In this section I will review a number of circulatory reflexes that have been studied in relation to external stimuli, and I will suggest that the notion of functional utility also applies to the circulation.

2.1. The baroreflex. The prime example of a cardiovascular reflex is the baroreflex. The baroreflex has two major components, a cardiac component and a vascular component. Although neither is fully understood, the general principle of each is well known: When the mechanoreceptors in the carotid sinus or the aortic arch are distended, they emit signals that stabilize or "buffer" the blood pressure. The signals normally evoke responses of the heart and selective components of the vasculature (see Simon & Reidel 1975), which result in changes in these organs that bring the blood pressure back to the prestimulus level. It is important to note that, although these reflexes usually operate in concert, there are circumstances under which the cardiac and vascular components function independently (Mancia, Ferrari, Ludbrook & Zanchetti 1980). The question I wish to address here is how these reflexes behave in response to standardized signals in the presence of other stimuli that cause cardiovascular responses incompatible with the baroreflexes.

A number of investigators have studied the cardiac component of the baroreflex when the animal is responding to other imperative stimuli. Most have shown that the baroreflex is modified when it is pitted against other cardiac-specific stimuli. Bristow, Brown, Cunningham, Howson, Petersen, Pickering & Sleight (1971) have reported that the sensitivity of the reflex is attenuated during dynamic exercise. Melcher & Donald (1981) and Walgenbach & Shepherd (1984) have questioned the findings of Bristow et al. (1971), but even if one accepts their measure of baroreflex sensitivity, they still found that the set point of the reflex (rather than the sensitivity, as in the case of Bristow et al.) was modified during dynamic exercise. Stephenson, Smith & Scher (1981) studied the sensitivity of the baroreflex in a range of situations and found that it did vary systematically across conditions: It was greatest during sleep, least during mild exercise, and intermediate during periods of food acquisition (pressing a lever to release applesauce) or actual eating. Brooks, Fox, Lopez & Sleight (1978) have shown that the baroreflex sensitivity is attenuated if the subject is performing a mental arithmetic task. Coote, Hilton & Perez-Gonzalez (1979) studied the cardiac and vascular components of the baroreflex during periods when the defense reaction was elicited by electrical stimulation in the hypothalamus. They found that it was possible to inhibit not only the cardiac component but also the vascular component of the baroreflex under appropriate stimulation conditions. In their conclusions they emphasized that "'the activating system' [of the brain stem defense areas] can directly inhibit the 'deactivating system' with which the baroreceptor afferent pathway is connected . . . . [and that] under appropriate experimental conditions, exactly the reverse is found, i.e., inhibition of alerting by the 'deactivating system.'" (pp. 558–9). They concluded, as I do, that the interaction among several conflicting inputs to the cardiovascular system is a function of the conditions under which the inputs are presented (see also Hilton 1980). This notion is further documented in a study by Baccelli, Albertini, Del Bo, Mancia & Zanchetti (1981). They studied the baroreflexes in the cat during fighting and proposed that "neurogenic influences active during natural fighting behaviors . . . may centrally block the existing inhibitory influence exerted by the sinoaortic reflexes on the circulatory system" (p. H428).

2.2. Other reflexes. The baroreflex is not the only stimulus-specific response system shown to be sensitive to the environmental conditions under which it is elicited. Several investigators have reported that the diving reflex can also be shown to be conditional. For example, Blix, Rettedal & Stokkan (1976) noted that "if the animal [a duck] is excited or unadapted to the experimental conditions these initial responses [the bradycardia] might fail to appear" (p. 482); Kanwisher, Gabrielsen & Kanwisher (1981) have reported that in the Canada goose and the cormorant, the diving reflex can be elicited in the naive animal but does not appear in an animal trained to dive. Another example of the fact that the cardiovascular adjustments to environmental stimuli are conditional is the interaction between the reflex metabolic adjustments of the circulation to dynamic exercise and the reflex, nonmetabolic adjustments to thermal stress. Nadel, Cafarelli, Roberts & Wenger (1979) and Nadel (1980) studied the effect of heat stress and the correlated effect of fluid volume depletion on the cardiovascular responses to exercise. The problem is easily stated: During exercise the cardiac output must be shunted to working muscles to maintain their metabolic requirements, while during heat stress the cardiac output must be shunted to the skin to facilitate cooling. Because cooling of the blood decreases the efficiency of working muscle and fluid volume depletion reduces the total blood volume and exacerbates the interaction between the metabolic and nonmetabolic requirements of the circulation, how does the cardiovascular system balance these factors? The evidence points strongly to the conclusion that the two reflexes are not balanced! Under the experimental conditions studied by Nadel et al. (1979), thermal balance is sacrificed in order to maintain work; skin blood flow is subordinated to muscle blood flow. Nadel's interpretation of his findings is similar to those I noted above for the integration of the baroreflex with the defense reaction: "When regulatory systems that share common effectors are presented with extreme conditions, the controlling and integrating mechanisms must search for the optimal compromise" (1980, pp. 1495–6). As is true in all the other examples of conditionality cited above, the "controlling and integrating mechanisms" lie in the central nervous system.

There are still other examples one could cite to document the fact that the responses of the circulation are conditional – e.g., Skinner & Entman (1975) have shown that the latency of ventricular fibrillation following coronary artery occlusion in the pig can be increased by adapting the animal to the laboratory. However, it should be clear from the above examples that over a wide range of reflexes and under a wide range of experimental conditions the reflex adjustments of the circulation are condi-

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tional and not static, and the integration and regulation of the responses is made in the central nervous system. This integration parallels the integration one sees in somatomotor reflexes; and, at least at the level of reflex integration, the circulation is no different from any other motor system whose behavior is controlled and regulated by the central nervous system: The factors determining which among several incompatible responses occur are the environmental contingencies present at the time the behavior is occurring and the functional utility of the reflex in relation to the total behavior.

3. Stimuli as cues

As noted above, a number of investigators have come to similar conclusions: Circulatory reflexes are not static but depend on environmental conditions at the time they are elicited. In order to account for this conditional variation in response, these investigators have invoked such factors as "appropriate experimental conditions," "neurogenic influences," and "search for optimal compromise." However, these factors can hardly be considered mechanisms: What does "appropriate" mean? How did the "influences" come about? And what criteria does the central nervous system use to "search for optimal compromise"? Obviously, there are only two possible mechanisms, and these are not mutually exclusive. One possibility is that the integration among reflexes is prewired, that is, regardless of conditions, certain reflexes will always dominate over others. The second mechanism would be that the stimuli eliciting the reflexes acquire secondary significance as a result of experience, that this significance determines the behavior the animal will emit, and that the resultant behavior is integrated – that is, in the awake animal the cardiovascular responses are components of the overall behavior of the animal and are determined by the situation and by prior experience. There certainly is strong suggestive evidence for the first mechanism. For example, the interactions between the cardiovascular responses to exercise and to heat are likely to be inherently hierarchical. However, it is difficult to see how the sensitivity of the dive reflex to training or the latency of ventricular fibrillation following coronary artery occlusion as a function of adaptation to the laboratory can be prewired. In this section I will examine some of the research that has shown that the reflexes elicited by stimuli change systematically as a result of experience.

3.1 Experimental models of cardiovascular conditioning. There are two kinds of experimental models that have been used to demonstrate that cardiovascular responses elicited by specific stimuli can be modified by training. One model uses classical conditioning techniques to modify cardiovascular responses; the other model uses operant techniques to produce somatomotor behavior that also generates concomitant changes in the cardiovascular system. It would be not only pointless but impossible to review all of the studies that could be included in this section. Detailed reviews have recently been published (Cohen & Randall 1984; Engel & Schneiderman 1984), and the interested reader should consult these for introductions into that vast literature. The papers I have chosen for review here were selected to document the fact that stimuli that elicit cardiovascular reflexes can also acquire secondary meanings as a result of associative conditioning; and that these acquired attributes will be associated with major changes in the behavior of the circulation.

Most of the studies of classical conditioning of cardiovascular responses have followed a common pattern. The investigators have selected some neutral signal – for example, an audible tone – and paired this signal with an aversive signal – for example, an electric shock to some part of the animal's body – and then shown that after some number of pairings, the neutral signal is capable of eliciting reliable cardiovascular responses that differ significantly from those it elicited prior to training. Thus, these studies have demonstrated that the meaning of the neutral cues can be changed by training; that the behavior of the circulation changes concomitantly; and, therefore, that the effect of the neutral cue is conditional on the learning history of the subject. Randall, Cottrill, Todd, Price & Wachtel (1982) have shown that monkeys can be trained to discriminate between a pulsating 3.4 kHz tone and a steady tone when the former is always followed by electric shock (in the trunk area), and the latter is never so associated. The tone followed by shock (aversive or unconditional signal) becomes reliably associated with increases in mean blood pressure (8%) and cardiac output (28%) that are largely the result of increases in heart rate. Peripheral resistance, of course, falls. The steady tone is not associated with any reliable changes in cardiovascular response. Subsequent studies of regional blood flow have suggested that the drop in vascular resistance is mediated by the beta-adrenergic, vasodilatory system. This experiment underscores a number of conclusions: (1) The cardiovascular responses noted above are unlikely to be inherent properties of the conditional signals (tones), although they could be inherent in the shock or in the motor behavior associated with the preparation for the shock; (2) the cardiovascular responses are integrated, reliable behaviors; (3) neutral signals, such as tones, can acquire the capacity to elicit organized behavioral adjustments (including cardiovascular ones) to inescapable aversive signals. Further evidence of integration among the acquired cardiovascular responses comes from a study of aversive conditioning in the dog by Billman & Randall (1980). Once again, using discriminable tones paired with shock, these investigators found significant increases in mean aortic pressure, instantaneous rate of change of blood pressure in the left ventricle (dp/dt), and heart rate. Coronary vascular resistance (measured during late diastole) rose shortly after the onset of the shock-associated tone and then fell subsequently, but before the onset of the shock.

3.2. Differentiation of conditional and unconditional responses. Given that the tone associated with shock elicits cardiovascular reactions, some investigators have questioned whether the response to this conditional signal is identical to the response to the unconditional signal. In order to analyze this question, Kadden, Schoenfeld, McCallough, Steele & Tremont (1980) conditioned heart rate and blood pressure in monkeys using a visual conditional signal and tail shock. They found that the heart rate response to the conditional signal was typically a ta-

chycardia followed by a bradycardia, as was the response to the unconditional signal. Blood pressure usually rose following the conditional signal and then fell almost immediately after the shock. These data indicate that the cardiovascular responses to the conditional and aversive stimuli are not identical. It should be noted that the aversive signal always follows the conditional signal; thus, in a sense, the aversive signal is itself conditional on the antecedent, conditional signal, and the response it elicits must be considered a complex one reflecting not only the aversive signal but also the antecedent state of the circulation.

In an effort to identify some of the neural mechanisms mediating some of these effects, Schoenfeld, Kadden, Tremont, McCullough & Steele (1980) gave some of the same animals various combinations of atropine, phentolamine and propranolol during conditioning trials. It was of particular interest here that they could block the response to the conditional signal but that this blockade did not necessarily eliminate the response to the aversive signal. These data are further suggestive evidence that central nervous system's control of the response to the conditional signal may be different from that of the response to the aversive signal.

The relationship between the conditional and unconditional signal was also examined by Randall, Kaye, Randall, Brady & Martin (1976). In their study of monkeys, they compared the response to a 3.4 kHz tone followed by shock to the trunk with the response to a 900 Hz tone followed by food. In contrast to the pharmacological denervation methods used in the Schoenfeld et al. (1980) study, Randall et al. surgically denervated the hearts of their animals. They measured heart rate, left ventricular systolic pressure and left ventricular dp/dt. They found the following: (1) Denervation largely eliminated the heart rate and dp/dt response to both the conditional and unconditional signal. However, there was a small, reliable increase in both of these responses that began shortly after the onset of the conditional signal and continued until well after the offset of the shock. They interpreted this as an unconditional catecholamine response to the conditional signal, referring to it as an "emotional stress." Regardless of how one labels the effect, it is clear that the response to the conditional signal can affect the response to the unconditional signal because it is well known that cardiovascular responses will vary nonlinearly in relation to their current state (Levy & Zieske 1969; McDonald 1974, pp. 351–88). (2) The left ventricular pressure responses following denervation were attenuated but qualitatively similar to the responses prior to denervation. Just as in the Schoenfeld et al. study (1980), in which systemic pressure was recorded, the pressor response to the conditional signal was a rise, whereas the response to the unconditional signal was a fall; however, in this case there was a subsequent rise in pressure.

These data show once again that the response to the unconditional signal is not identical to the response to the conditional signal, suggesting that this effect occurs, at least in part, in the vasculature because the differences in response to the conditional and unconditional signals are similar in the innervated and denervated heart. The pattern of effects with the conditional and unconditional food stimuli is similar to that with the aversive stimuli: Denervation abolishes the heart rate and dp/dt responses but not the pressor responses, and the pattern of responses following the conditional signal is different from that following the unconditional signal. Another study that found evidence that the response to the conditional signal can interact with the response to the unconditional signal was that of Gold & Cohen (1981; 1984). They used light as the conditional signal, foot shock as the unconditional signal, and pigeons as subjects. They observed a reliable decrease in the rate of discharge of vagal cardiac neurons in the naive animal in response to the visual signal. During training, this effect became greater, paralleling the acquisition of the conditioned tachycardia, which also included an increase in sympathetic activity.

3.3 Clinical models. A number of investigators have been interested in classical conditioning procedures because they believe that these might be useful models for studying clinically relevant problems. Typical among these are the studies by Lown, Verrier & Corbalan (1973). Their interest is in the clinical problem of sudden death mediated by a ventricular arrhythmia. They first developed an experimental model for the production of a ventricular arrhythmia in the dog and then used a classical aversive conditioning procedure to see whether this affected the vulnerability of the heart to such an arrhythmia. Although their protocols are complex and they do not provide statistical analyses to support their conclusions, their findings are consistent with other data presented here: When control animals tested in their home cage are compared to experimental animals tested in the device in which they received uncontrollable electric shocks, the experimental animals have lower thresholds for repetitive ventricular beats than the control animals (Lown et al. 1973). Furthermore, this same group showed that when this protocol is introduced to animals that have also been given permanent myocardial infarctions (by chronically inflating a balloon catheter implanted in the left anterior descending coronary artery), the dogs in the conditioning paradigm are all more likely to develop ventricular arrhythmias at lower thresholds than are the control animals (Corbalan, Verrier & Lown 1974).

3.4 Baroreflex interactions. As noted above, the baroreflex can be modulated by concomitantly presented stimuli. Using classical conditioning procedures one can also test the converse question: What role does the baroreflex play in modulating the conditional responses of the circulation to aversive stimuli? Nathan, Tucker, Severini & Reis (1978) tested two groups of cats. In one group the nucleus of the tractus solitarius (NTS) was lesioned; in the other only a sham lesion was performed. Since the NTS is known to be a primary receiving area for inputs from the sinus and aortic nerves in the cat (Spyer & Jordan 1980), the lesioned animals no longer had functional baroreflexes. Animals in both groups were then classically conditioned with tones of different frequencies as the conditional stimuli and shocks to the trunk as the unconditional stimuli. They found that the lesioned animals emitted pressor responses to the shock-paired, conditional signal which were about five times as great as the responses emitted by the sham-lesioned animals to the same conditional signal. Thus, these data show that just as significant environmental stimuli can modulate the baroreflex, so also can the baroreflex modulate the response to

environmental signals. These data are further evidence that cardiovascular responses are integrative components of behavior and not passive reflexes that merely occur in response to adequate stimuli.

4. Cardiovascular responses as mediators of behavior

In the previous two sections, I reviewed some of the findings showing that the responses of the circulation are not isolated reflexes but integrated components of behavioral acts. In this section I wish to raise the question: Are cardiovascular responses inherently reactive or are there circumstances under which these effects can be made proactive? In other words, do the cardiovascular responses occur *pari passu* with somatomotor behavior, as many investigators have proposed (for example, Rowell 1980), or can these effects be modulated independently of the somatomotor responses? If cardiovascular responses are necessarily consequences of somatomotor responses then this would suggest that the circulation is wholly reflexive in its actions and that preparatory responses of the circulation *per se*, if they occur at all, must be minimal. If, on the other hand, cardiovascular responses can be emitted in anticipation of environmental events, then, within the physiological and anatomical constraints inherent in its structures, the cardiovascular system can be said to have a role in purposive behavior comparable to that ascribed to the somamotor system.

4.1 Heart rate as operant behavior. One demonstration that cardiovascular responses can become proactive would be to show that strong stimuli, those widely accepted as elicitors of highly specific cardiovascular responses, can have their effects reversed through appropriate training. I raised the question of stimulus specificity earlier in relation to studies of classical conditioning that used electric shock as the aversive stimulus. Those experiments had shown that the cardiovascular responses were not inherently elicited by the conditional signals because there were large differences between the responses to the conditional signals before and after training; there were also large differences between the responses to the shock-paired and nonshock-paired conditional signals after training. However, it is still possible that the unconditional signal (usually electric shock to the body) somehow influenced the cardiovascular responses, even though other research has shown that the response to the conditional signal was different from the response to the shock.

Several years ago, my colleagues and I developed an experimental model designed to test this question further. We trained monkeys to speed or slow their heart rates to avoid an electric shock to the tail. The main feature of this preparation was that the response that determined the occurrence of the shock was the monkey's heart rate. Briefly (see Engel & Gottlieb 1970 for a detailed description of our techniques), our protocol had the following features: (1) The monkey was maintained in a primate chair set in a primate booth. The animal was prepared with a chronic, indwelling arterial cannula, which we could keep for months. (2) Animals were trained to slow and speed their hearts to avoid a 10 mA, 0.45 sec tail shock. The shock (aversive stimulus) was the same whether the animal had to slow or to speed its heart. The discriminative stimuli were lights (red = slow; green = speed), and the correct response was signalled by a yellow light, which was on when the animal was performing successfully and off when the animal failed to emit the correct response. Whenever the animal failed to perform correctly it would receive the tail shock, followed by additional shocks at the rate of one each 8 sec, until the animal performed successfully again. (3) In the experiments described here, the sessions during which the animal was tested were 2,048 sec in duration. (4) By using an operant conditioning procedure in which the same aversive signal (tail shock) was used, we could test whether the responses in heart rate and blood pressure were inevitable consequences of the shock or whether the animals could, in fact, modulate their heart rates appropriately to avoid the shock.

In order to minimize any bias in the procedure, each animal was studied during four sessions each day. During two sessions the animal had to speed its heart rate to avoid shock and during the other two it had to slow the rate. Furthermore, the sequence of these sessions was counterbalanced over days to minimize the likelihood that the animal would develop response predispositions during the baseline periods that might influence its performance.

Figure 1 presents the averaged performance for five animals (the data are taken from a study by Gottlieb & Engel 1979). The animals were clearly very proficient at maintaining heart rate appropriately, thereby consistently avoiding shock. Several additional points are worth noting: (1) The performance for a single animal is very similar to that for the group seen in Figure 1. (2) The cardiac response patterns during the speeding condition and the slowing conditions are different – animals tend to achieve and maintain a slower heart rate more rapidly than they do a faster heart rate. (3) The responses in blood pressure tend to be inconsistent – systolic and diastolic pressures tend to behave differently and there is usually little or no rise in either response regardless of condition

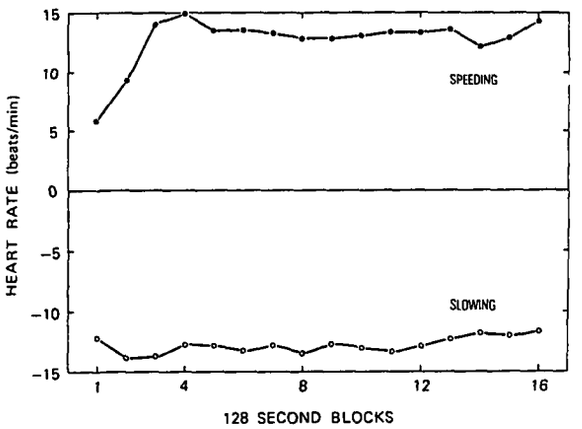

Figure 1. Average change in heart rate from baseline for five animals. Each animal participated in 20 slowing and 20 speeding sessions, 4 sessions/day. Daily sessions were counterbalanced with 2 slowing and 2 speeding sessions. Baseline duration was 512 sec and session duration was 2,048 sec. The abscissa is divided into 16 128-sec time units to show the progression of performance, but the session itself was continuous for the full 2,048 sec.

(heart rate slowing or speeding). (4) The effects noted here are not mediated by baseline differences; for example, the average baseline heart rates for the five animals depicted in Figure 1 were 156.6 beats/min (speeding) and 152.4 beats/min (slowing).

Although the animals in the experiments cited above showed reliable performances during the slowing and speeding condition and were thus able to differentially control their heart rates, there was still the possibility that there were important effects in relation to the shock *per se* that could not be seen in Figure 1. In order to analyze the degree to which the animals were responding to the shock appropriately, we carried out a detailed analysis of the performance of another group of animals during the 30-sec interval preceding a shock and the 30-sec interval following the shock (Engel 1974). Because this analysis focused on cardiovascular behavior in relation to shocks, the performance prior to the shock was selected to be incorrect (otherwise the animal would not have received a shock). The results in Figure 2 show that the animals were able to make an appropriate response rapidly and reliably. Furthermore, despite rather large "escape" responses (heart rate responses that turned the yellow light on and prevented further shocks), there were no pressor responses. Thus, the animals learned to discriminate their cardiac responses appropriately and to emit these as needed without major changes in other cardiovascular effects.

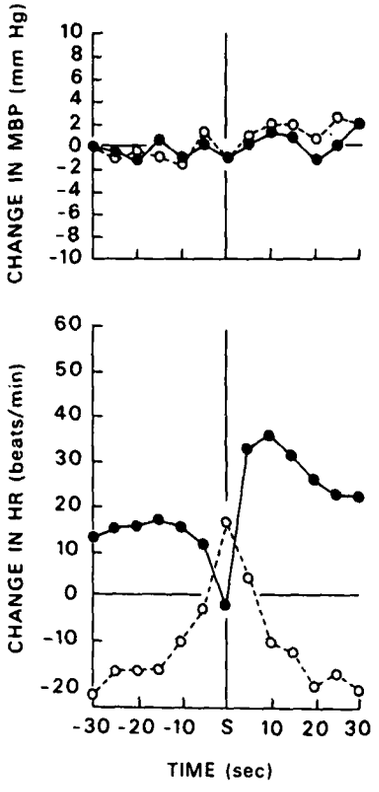

Figure 2. Average heart rate (HR) and mean blood pressure (MBP) responses relative to baseline for three animals during heart rate slowing sessions (dashed lines) and heart rate speeding sessions (solid lines). Data were averaged at 5-sec intervals and illustrate the post-shock escape behavior of the animals. Note that there are very large changes in heart rate prior to and following tail shock but no concomitant changes in mean pressure.

In order to assess the extent of the control our animals were exerting on their cardiovascular functions we studied animals in a number of situations in which we created competing demands on the circulation. In one such study, we elicited baroreflexes pharmacologically, using either phenylephrine (which raises the blood pressure, thereby reflexively eliciting a bradycardia), or nitroglycerin (which lowers the blood pressure, thereby reflexively eliciting a tachycardia). Our hypothesis was that when the animal was proactively raising its heart rate to avoid shock it would attenuate the reflex sensitivity of the nitroglycerin-elicited cardiac component of its baroreflex, and when it was proactively lowering its heart rate to avoid shock it would attenuate the phenylephrine-elicited cardiac component of its baroreflex sensitivity. Both predictions were supported: Each of the three animals modulated the sensitivities of their baroreflexes in the hypothesized directions during the cardiac conditioning experiments (Engel & Joseph 1982).

4.2 Operant training can change a classically conditioned heart-rate response. In order to examine the interaction between conflicting demands placed on the circulation we also studied the effect of our operant cardiac training procedure on the cardiovascular responses acquired through classical conditioning. First, we (Ainslie & Engel 1974) trained animals in an experimental paradigm similar to that used by Randall et al. (1982) to discriminate between a click frequency of 20/sec and one of 2/sec. One of the frequencies was always followed by a tail shock (10 mA, 0.45 sec), whereas the other was never associated with a tail shock. In the case of two of the animals, the shock-associated clicks were 2/sec and for the other two it was 20/sec. During this phase of training, each session began with a 512-sec baseline period followed by 4 continuous 512-sec test blocks. During each test block, first the 2/sec click sounded for 128 sec, then there was a 128-sec period of silence, then the 20/sec click sounded for 128 sec, and, finally, there was another 128-sec period of silence. As Randall et al. (1982) and others have reported, the animals soon learned this task and responded to the shock-paired conditional signal relative to the nonshocked conditional signal with a tachycardia and a pressor response.

After the animals had been taught this task, two were trained to slow their heart rates to avoid the shock, two to speed them. These operant training sessions always began with a 512-sec baseline period followed by a 2,048-sec session, during which the animal was required to slow or speed its heart rate. Once the animals had acquired these skills, they were retested in the classical conditioning experiment. Then they were trained in the joint task, that is, they were placed in a situation that required them to speed or slow their hearts and, at appropriate times, clicks were superimposed on this behavior (the 4 blocks of 512-sec clicks described above were superimposed on the 2,048-sec period of operant heart rate conditioning). Finally, the animals were retested in the clicks-only situation.

Figure 3 summarizes the main findings (which are reported in considerably greater detail in Ainslie & Engel 1974): (1) The response to the shock-paired clicks relative to the nonshocked clicks is a tachycardia and a pressor response. (2) When the clicks are superimposed on the

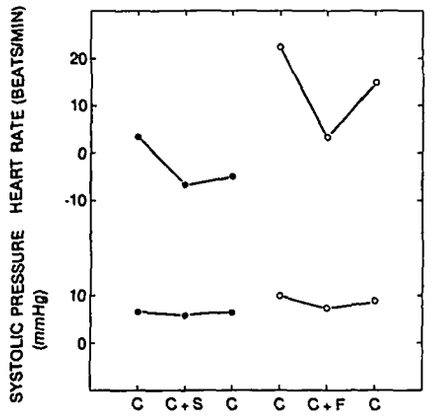

Figure 3. Average differences in heart rate and systolic blood pressure for four animals (two in each group). All animals were first tested in the classical conditioning situation (C). Two were trained in the combined slowing and classical procedure (C + S) and two in the combined speeding and classical procedure (C + F). Then all were retested in the classical procedure (C). Each point is the difference between the response to the shock-related clicks and the nonshock clicks. Each animal was trained first in the classical conditioning procedure, then in the operant procedure (neither shown in this figure). They were then retested in the classical conditioning procedure, in the combined procedure, and, finally, in the classical conditioning procedure again. Each point is the average of 100 or more pairs of trials during which clicks of different frequencies were presented. The clicks were reliably and differentially either followed by shock or never followed by shock.

cardiac control conditions, the animals respond selectively: (a) Animals that are speeding their hearts to avoid shock also speed to the clicks and raise their blood pressures; (b) animals that are slowing their hearts to avoid shock slow even more to the clicks, which are always followed by shock relative to the nonshocked clicks. However, they still emit a pressor response to the clicks. (3) When the animals are returned to the clicks-only experiment, they retain the responses acquired during the combined condition (that is, animals trained to speed heart rate emit a tachycardia and a pressor response and animals trained to slow it emit a bradycardia and a pressor response). It should be emphasized that each of the conditions was tested extensively – well over 100 trials/animal/condition – and the results are highly significant. They show that the animals are capable of acquiring very precise cardiovascular skills and of performing these as needed.

4.3 Dissociation of somatomotor and cardiovascular behaviors. Smith, Astley, DeVito, Stein & Walsh (1980) have also provided some important data on the effect of electric shock on cardiovascular reactivity. They trained baboons to emit a socalled conditioned emotional response. The conditional emotional response is defined by the following procedures: (1) Animals are trained to press a lever to obtain food. (2) After this skill is well established, the lever-press behavior is paired with clicks of different frequencies. One frequency indicates that an inescapable shock will come at the end of the click interval and the other frequency, readily discriminable from the first, is never followed by shock. After a few such pairings, when the click associated with shock is turned on, the animal will stop pressing the lever for food, until finally the click is turned off and the shock is received. During the period when the motor behavior (pressing) is suppressed, there is evidence of cardiovascular behavior (increases in heart rate, blood pressure, and cardiac output). The question Smith and his colleagues asked was whether these two classes of shock-elicited responses (suppression of bar pressing and cardiovascular reactivity) could be dissociated. They found that lesions in specific regions of the hypothalamus could abolish the cardiovascular components of the conditioned emotional response and leave intact the somatomotor components. What is especially significant is that the lesions did not prevent the cardiovascular responses to other behaviors, such as dynamic exercise or feeding. Thus, this experiment showed that, at least for the neural circuits involved in the conditioned emotional response, it is possible to separate the expression of the shock-elicited cardiac response from other expressions of stimulus-elicited cardiac response.

4.4. Learned control of the cardiovascular adjustments to exercise. The findings reviewed above suggest that animals can learn to modulate their cardiovascular responses and that the acquired responses are unlikely to be specific attributes of the stimuli. Even a stimulus as compelling as shock – which many investigators have characterized as a stress and which is widely believed always to elicit an increase in cardiovascular reactivity – can either become a reinforcer for the opposite effect or can be dissociated from its usual effect. However, electric shock is not the only compelling stimulus eliciting reliable cardiovascular responses that can be modified under appropriate experimental conditions. There are now a number of studies showing that subjects can be trained to modulate cardiovascular adjustments to exercise. We have carried out two studies with humans which show that under appropriate experimental conditions normal subjects (Perski & Engel 1980) and conditioned athletes (Perski, Tzankoff & Engel 1985) can learn to attenuate the tachycardia of dynamic exercise. Other investigators have reported comparable results for dynamic (Goldstein, Bardy & Ross 1977) or isometric (Clemens & Shattock 1979) exercise. In our experiments, we trained subjects to exercise on a bicycle ergometer at either ~50% or ~70% of maximal heart rate. The control group exercised without any instructions or feedback on cardiac performance; the experimental group exercised while observing visual displays of their beat-to-beat cardiac rate with instructions to attempt to maintain heart rate as low as possible while keeping their exercise performance unchanged. After several days of testing under these conditions, the control subjects were given the same instructions as the experimental subjects as well as access to visual displays of their cardiac activity. The results of these two studies are summarized in Figure 4: (1) Subjects who had access to visual displays were able to attenuate their heart rates reliably; subjects not so informed did not modify their rates. (2) Although subjects did slow their hearts, they did not modify their blood pressures. (3) The rate-pressure product (heart rate × systolic pressure), a measure of left ventricular work and of O_2 consumption ($\dot{V}O_2$) followed heart rate.

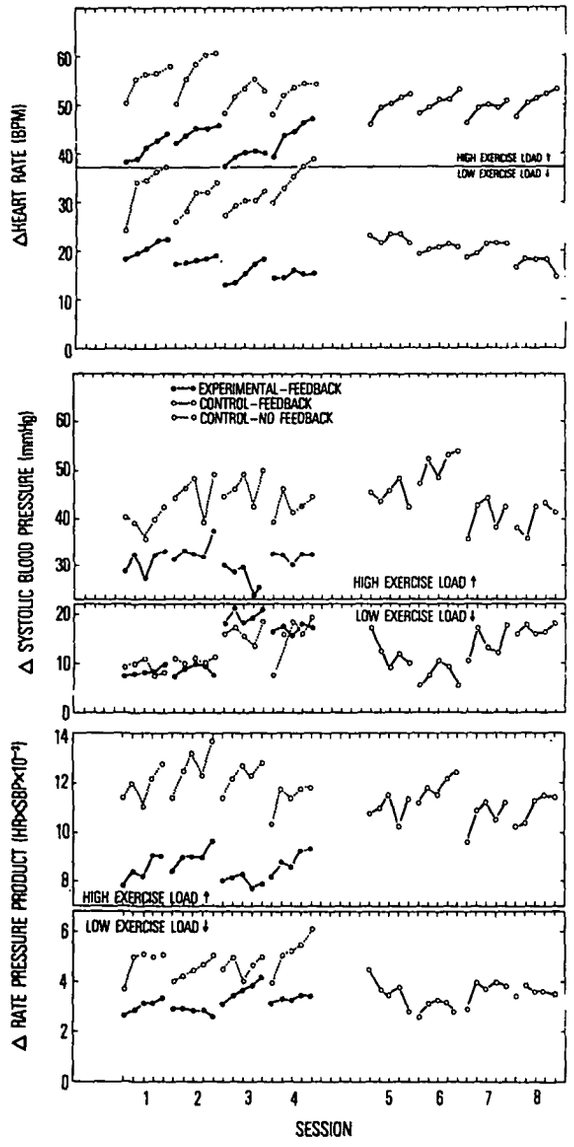

Figure 4. Average heart rate, systolic blood pressure, and rate-pressure product responses for four groups of five subjects each. Two groups exercised at a high load (~ 70% of maximal heart rate), two at a low load (~ 50% of maximal heart rate). The experimental subjects were trained to attenuate their heart rates while exercising on a bicycle ergometer, whereas the control subjects exercised at the same workload and for the same duration. After completion of the first phase of the study (sessions 1 to 4), the control subjects were given combined exercise and heart rate slowing training. The experimental subjects had consistently smaller increases of heart rate and rate-pressure product than did the controls. When the control subjects were given feedback on their heart rates, they too significantly decreased their heart rates and rate-pressure products relative to their performances without feedback.

4.5 Central command as learned behavior. Experiments with humans are interesting and provide insight into potentially useful applications of various interventions. However, they are limited in that one lacks the ability to implement all desirable experimental controls. In order to study cardiovascular regulation during exercise in greater detail, we have recently developed a nonhuman primate model for study. Because the data are not yet published, I will describe the procedure and results for one animal in some detail.

We first trained a monkey to slow its heart rate, as I described above. Then we taught it to lift a weight repeatedly. The weight was 8.2 kg (the animal weighed 8.0 kg), and the distance it had to raise the weight was 4.5 cm. In order to satisfy the experimental conditions outlined below, the animal had to lower and raise the weight repeatedly (the experimental duration was 1,024 sec). The experimental conditions were arranged so that if the monkey did not lift the weight within 2 sec after a previous lift, a clicker would begin sounding, and after 4 sec the monkey would receive a tail shock. If the animal failed to lift the weight within another 4 sec, it would receive a second shock, and this protocol continued throughout the session. After the monkey was exercising reliably and slowing its heart rate reliably, we combined the two protocols – that is, the monkey was required to exercise and at the same time attenuate its heart rate (note the similarity between this protocol and the one used by Ainslie & Engel described above).

The results are based on 74 sessions, half exercise-only and half combined exercise and heart rate slowing; four daily sessions were counterbalanced over days. It should be emphasized that by this stage of the study, the animal had been in the program for almost one year and its exercise performance and combined heart rate slowing and exercise performance had become very reliable. During the 74 sessions on which the results cited below are based, the animal lifted the weight 20 to 30 times/min. During the exercise-only sessions, it received an average of 0.01 tail shocks/min for failing to lift the weights according to schedule. During the combined sessions, it received 0.03 shocks/min for failing to lift the weights according to schedule and 0.06 shocks/min for failing to attenuate its heart rate appropriately.

Figure 5 shows the relationship between cardiovascular performance and $\%0_2$ in the expired air relative to room air. The point on each curve is the mean level of reactivity from baseline for each of the variables graphed; the line drawn through each point is the line of best fit through the 37 pairs of data points. The main findings were: (1) There were significant differences in average change in heart rate (bpm) (40.4 vs. −0.7), and slope (bpm/$\%0_2$) (4.46 vs. 1.52) between the exercise only and combined sessions, respectively. (2) Systolic pressure (mm Hg) changes did not differ (16.3 vs. 14.5), but the slopes (mm Hg/$\%0_2$) were different (7.05 vs. 1.40). (3) The rate-pressure products paralleled the heart rate effects; both the changes (9.65×10^{-3} vs. 2.72×10^{-3}) and the slopes (2.31 vs. 0.56) were significantly different. Thus, these findings were similar to those for the human subjects. The animal was able to attenuate its exercise-induced heart rate response when the heart rate control condition was added to the exercise condition. During the combined condition, the monkey's cardiovascular system functioned more efficiently for the same workload than it did during the exercise-only condition. Although this is a continuing program, we have completed the study of three animals (including the one just described), and all showed similar patterns of behavior (Talan & Engel, in press).

A number of investigators are exploring the relationship of somatomotor to cardiovascular behavior during exercise. Many of these studies suggest that cardiovascular responses can be either reactive or

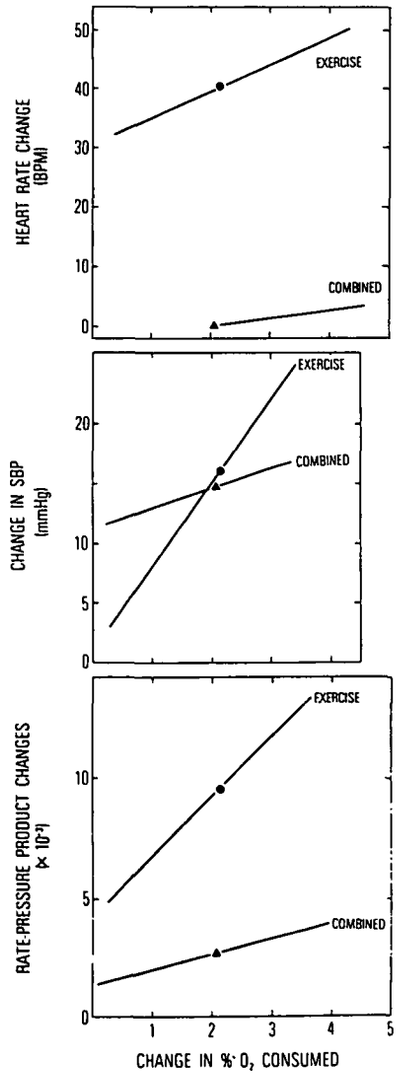

Figure 5. Average heart rate, systolic blood pressure and rate-pressure product responses during exercise and combined heart rate slowing and exercise sessions. The animal participated in 37 sessions – session duration = 1,024 sec – under each condition. The abscissa is % change from baseline of O_2 extracted from room air. The point on each line is the mean level for the variables and the slope of the line is the slope of the line of best fit through the 37 pairs of points.

proactive. In their recent review of the role of skeletal muscle afferents in the cardiovascular adjustments to exercise, Mitchell & Schmidt (1983) conclude that "The dominant concept has been that pressor and depressor reflex cardiovascular responses are caused by specific types of afferent fibers from skeletal muscle. It is now evident that this hypothesis is overly simplistic" (p. 652). In particular, they cite experiments showing that reflexes initiated from peripheral receptors play an important role in the cardiovascular adjustments to exercise; however, there is also considerable evidence that central neural activity initiates both somatomotor and cardiovascular behavior. What is not yet clear is whether the somatomotor effects are necessary or merely sufficient to elicit the cardiovascular responses.

Hobbs (1982), working with Smith's group, is studying the central neural mechanisms mediating the cardiac adjustments to exercise. In particular, he is studying the extent to which the central motor command and the cardiovascular command can be isolated. Clearly, this question is directly relevant to my question about the degree to which situation-specific cardiovascular and somatomotor responses can be dissociated. Hobbs trained baboons to emit a sustained isometric contraction of the arm. After they had acquired this skill, an arterial cannula was inserted to measure intra-arterial pressure and the animals were given electrolytic lesions in subthalamic nuclei known to be associated with the integration of cardiovascular, respiratory, and somatomotor responses during exercise (Smith, Rushmer & Lasher 1960; Eldridge, Millhorn & Waldrop 1981). The question Hobbs asked was: Are these integrated responses inevitably linked or can they be dissociated? The results of this experiment provided further support for the notion that the cardiovascular responses can be dissociated from somatomotor and pulmonary effects because the animals were able to perform the isometric response. However, there was not the concomitant rise in blood pressure that had occurred prior to lesioning. Control experiments showed that the animals were still capable of responding to other stimuli – for example, startle – with rises in blood pressure. Thus, the lesion did not prevent the expression of cardiovascular responses, although it might have interfered with specific pathways associated with the exercise response.

We are also very interested in the mechanisms underlying central command. However, our strategy for addressing this very complex issue has been to see whether an animal trained to modulate its heart rate can do so in the face of imperative electrical stimulation of the brain areas known to elicit cardiovascular responses. If an animal can modulate its cardiac response in the face of imperative stimulation then, obviously, either it must be inhibiting the stimulus effect distal to the point of stimulation or influencing an output tract that is overriding the stimulus effect. In any case, if one can identify such areas, it may be possible to develop a functional map of the brain. We have reported one study in which we found clear evidence that there are a number of telencephalic and diencephalic areas that can be stimulated electrically to produce reliable increases in heart rate, which can be overcome by monkeys that are slowing their hearts to avoid tail shock (Joseph & Engel 1981). Figure 6 illustrates vividly the extent to which one animal was able to prevent the rise in heart rate consequent on stimulation of the posterior hypothalamus during a trial when it was slowing its heart rate. Note also that despite the attenuated heart rate response, blood pressure still rose in conjunction with the brain stimulation. Eventually we hope to combine this experimental protocol with the exercise protocol described above.

5. Discussion

I have tried, in this target article, to show that: (1) The reflex responses of the circulation are not static processes elicited mechanically in response to adequate stimuli; rather, they are highly variable, very sensitive responses to the environmental conditions under which they are studied. (2) The attributes of stimuli that make them

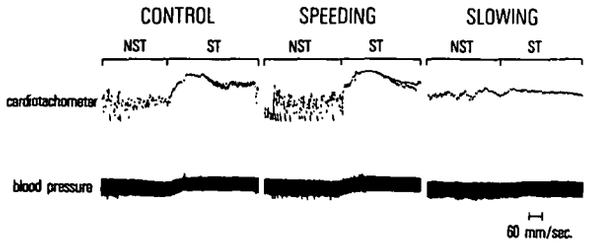

Figure 6. Heart rate and blood pressure tracings recorded during periods when the animal was in control, heart-rate-speeding, or heart-rate-slowing session. Each block is 128-sec long and divided into two 64-sec segments when the animal is either receiving electrical stimulation in its posterior hypothalamus (ST) or not (NST). Note that in the control and speeding sessions the animal responds to brain stimulation with a tachycardia and a pressor response; however, during the slowing session, there is no tachycardia but there is a small pressor response.

elicitors of cardiovascular responses need not be innate; in fact, most stimuli in the natural setting probably have acquired their elicitive properties through associative conditioning. (3) Cardiovascular responses are not necessarily reactive; there are a number of experimental circumstances under which they can be seen to be proactive – not only can they be elicited by adequate stimuli, they can be emitted to produce stimulation. On the basis of these findings, I am proposing that cardiovascular responses are aspects of behavior and obey the same rules as do other aspects of behavior: They can be elicited reflexes; they can be acquired reflexes; and they can be proactive responses, emitted as functional acts.

5.1. Possible selective factors in the evolution of cardiovascular behavior. A review of the phylogenetic development of the circulation strongly indicates that there is a close functional relationship between the circulation and other adaptive behaviors of animals, However, the role of the nervous system in this relationship is an evolving one. The circulation first appears in round worms, where it apparently evolved from the gut (Martin 1980). In many invertebrate species there is little evidence of neural control of the circulation. Yet, among the arthropods, as well as among the diverse species in which the circulation provides an important skeletal function, it is neurally regulated (Prosser 1973). In the primitive chordates, where gas exchange is primarily mediated through diffusion, there is very little involvement of the nervous system in the circulation (Randall & Davie 1980). But two major evolutionary trends, which probably strongly influenced the evolution of neural involvement with the circulation, appear in these animals. There was a decline in blood volume and an increase in blood pressure, and the blood flow distribution evolved from simple series circuits to complex, parallel vascular trees.

Both of these changes increased the need for integrating mechanisms. Among the fish, cardiorespiratory coupling is clear, albeit conditional. When the 0_2 concentration of water is low, there is a strong coupling of cardiac performance (primarily heart rate) and breathing; however, when the 0_2 concentration of water is high, there is no coupling (Randall & Davie 1980, pp. 73–74). As a matter of fact, one of the hypotheses about the evolution of terrestrial vertebrates is that the pressure came from an 0_2 deficiency in the water, which led to a high metabolic cost of ventilation. Obviously, this hypothesis implies that there is a powerful link between pulmonary, circulatory, and somatomotor behaviors and that respiratory drive acts as the primary mediator of behavior. Among other important factors mediating the evolution of neurocirculatory interactions are the first appearance of a double circulation and the first appearance of the sympathetic nervous system as a regulator of vascular function.

Among vertebrates, probably the most significant evolutionary pressures to involve the nervous system with the circulation occurred in conjunction with air breathing and the inevitable development of a double circulation. Among lizards, there is already strong evidence of proactive neural modulation of the circulation. These animals are intermittent breathers; during periods when they are not breathing their heart rates are slow and blood flow is largely shunted to the systemic circulation because of a high, neurally mediated resistance in the pulmonary artery (lizards have only one ventricle). When these animals begin to breathe, pulmonary resistance falls and blood is shunted to the lungs. At the same time, heart rate rises precipitously. What is especially interesting is that among some species of lizard this ventilation tachycardia occurs before the onset of breathing through central irradiation (Johansen & Burggren 1980, p. 104). These authors state that ventilation tachycardia is mediated through vagal activity but is not elicited from pulmonary or arterial receptors.

The most significant evolutionary development of the neurocirculation after the developments associated with the transition from water to air breathing is probably the transition from poikilothermy to homeothermy. This transition is correlated with the elaboration of vascular control by the sympathetic nervous system and the emergence of a number of central neural mechanisms for regulating blood flow distribution and for balancing the demands of temperature regulation against metabolic and other demands on circulation. Satinoff (1978) has proposed that thermoregulation involves multiple control systems that operate hierarchically and modulate both circulatory and somatomotor behaviors. Satinoff reviews a considerable body of data indicating that these integrated systems, under appropriate conditions, can function independently.

5.2. Isolated reflexes, integrated behaviors. In the Introduction, I cited Sherrington's studies on the interrelationships among reflexes. In particular, I noted his emphasis on the observation that the interactions among reflexes seem to be determined, in part at least, by a principle of functional significance. When two or more reflexes are pitted against one another, the resultant response need not be an average of the two responses; it can be just one or the other response. It is a paradox that Sherrington is so often cited for his brilliant conceptualization of the reflex but, at the same time, his admonitions about the limitations of the concept are overlooked. In his last years he even grew cynical about the reflex and is quoted by Lord Brain as having said, "The reflex was a very useful idea, but it has served its pur-

pose. What the reflex does is so banal. You don't think that what we are doing now is a reflex do you? No, no, no." (Swazey 1969, p. 163). I do not think that cardiovascular reflexes are banal, but I certainly believe (as most athletes and most sport physiologists probably also believe) that the cardiovascular system is capable of responding "for" as well as "to" the world around it.

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Cardiovascular behaviour: Where does it take us?

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There are no surprises, I imagine, in the idea that cardiovascular responses, and presumably other autonomic/endocrine system responses, can be regarded as "behaviour." It would be difficult to defend any semantic restriction that suggested otherwise.

I was interested in Engel's article because it made me think a bit more about the notion. It is a good idea and the evidence presented makes the case, but what can be done with it? I will comment in rather general terms.

1. Purpose and optimal patterns. The idea that somatic behaviour is purposive comes very naturally from observing the behaviour itself. Working one's muscles to extend the hand and point a finger makes obvious sense in a button-pushing experiment. But what about a change in heart rate or arterial pressure? Engel quotes Kanwisher et al. (1981), who have shown that trained ducks lose the bradycardic diving response. It can be argued that this marked bradycardia is part of an oxygen-sparing response whereby a reduced cardiac output passes between lungs and brain. If the bradycardia can be dispensed with, was it necessary in the first place? We really need to understand so much more about visceral behaviour before we can answer this sort of question. Until then one can always come up with something plausible, but only very rarely is the matter put to a test. For example, is it known whether the trained duck can dive for the same length of time as the naive duck? The same point is made en passant by Engel in Section 2.2 and I would imagine that he feels equally unhappy with these teleological arguments.

2. Parcels of behaviour. Much of the work on conditioned responses seems, to someone who is not particularly well read on the subject, to deal with parcels of behaviour: the response to feeding, to exercise, to pain, etc. Conditioning is demonstrated by the linking of one such packet to a previously neutral stimulus. The cardiovascular responses discussed here are mostly changes in heart rate and blood pressure. The first may involve changes in sympathetic or vagal activity or both, while similar blood pressures may result from an infinity of combinations of complex cardiac and peripheral alterations. There can be no way of seeing what is going on unless one has a lot more information than is generally presented. The trouble is that we need the idea of the parcel to describe what we are looking at, but unless it is defined in exact quantitative detail its subsequent recognition will sooner or later lead to dispute.

3. Mechanisms. Returning to the diving ducks. A very recent piece of work (Gabbott & Jones 1985), while confirming Kanwisher's observation on trained animals, also showed that bradycardia could be prevented in naive ducks by giving them pure oxygen to breathe before the dive. Is the result of training the alleviation of fear, or have the ducks learned to overbreathe when a forced dive is clearly imminent, or what? Again, in the work of Lown et al. (1973), were the conditioned dogs exhibiting an arrythmia avoiding behaviour, maybe manifest as increased vagal drive, or is it that a lower background of sympathetic activity leads to the unsurprising result? Incidentally, is it surprising that cats whose baroreflex responsiveness has been abolished (Nathan et al. 1978) show less buffering of the pressor response to anticipated pain?

If we need to get down to details of mechanism and dissect out the response parcels we will have to talk in terms of activities in specific neural pathways. Possibly Sherrington's quoted reference to the "banality" of the reflex had something to do with a similar realisation. The studies of Hobbs (1982) seem to be a helpful beginning.

4. Humanitarian caveat. So, I find the ideas put forward here useful but unsurprising. I must end on a note of protest, however. It would be dishonest not to say that this article made me extremely uneasy, to put it mildly. I don't think I can accept that the relatively modest conclusions pointed to by much of the quoted work justify the experiments. Why do those working in this area use the crude and repellant sledgehammer of the electric shock to the almost total exclusion of almost anything else? Can one learn much about cardiovascular, or any other, behavioural response from studying a laboratory artefact whose existence has consisted for over a year of attempts to avoid electric shocks by repeatedly lifting rather more than its body weight?

Behavioral stress and myocardial ischemia: An example of conditional response modification

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Engel provides a valuable and scholarly review of the cardiovascular behavior literature. His article is not only informative but, more important, it is thought provoking and should prove to be a potent stimulus for further research. I find that I am in almost total agreement with the major theses proposed. Like Engel, I believe that the circulation represents one component of an integrated series of responses known as behavior and, further, that the cardiovascular response elicited by an environmental stimulus does not represent a simple, static all-or-none type of response but a dynamic one that changes to meet the demands of the situation.

It has been demonstrated that the cardiovascular response to environmental stimuli can modify other reflex responses. For example, both exercise (Melcher & Donald 1981, and Walgenbach & Donald 1983) and "emotion" (Engel & Joseph 1982; Goldstein et al. 1977; and Stephenson et al. 1981) have been shown to alter (inhibit) the baroreceptor reflex. Conversely, Nathan et al. (1978) demonstrated that the cardiovascular response to an aversive stress was accentuated in cats in which baroreceptor afferent input had been eliminated by bilateral lesions in the nucleus of the tractus solitarius. Thus, responses to environmental stimuli can both modify and be modified by cardiovascular reflexes. It is my intention to present supplementary evidence in support of this concept.

Acute myocardial ischemia is known to elicit a variety of cardiovascular responses that are dependent to some extent on the location of the ischemic injury; anterior wall ischemia primarily activates sympathetic afferents that are excitatory and inferior posterior wall ischemia activates vagal afferents that are

inhibitory (Longhurst 1984). Thus, bradycardia and hypotension accompany posterior wall ischemia, whereas tachycardia and hypertension are frequently associated with anterior wall ischemia (Corr et al. 1976; Randall & Hasson 1978). If an aversive stress evokes a passive reflex response, then one might expect that the simultaneous activation of this reflex during myocardial ischemia would lead to an algebraic summation of the two reflex responses. Thus, one would predict that anterior ischemia, which is excitatory, would accentuate the cardiovascular response to stress, whereas posterior ischemia may attenuate the response. But this does not appear to be the case. In the absence of myocardial ischemia, aversive stress elicits a very consistent response pattern (Billman & Randall 1981). Briefly, a classical aversive conditioning paradigm was used as a model of controlled stress. The paradigm consisted of two 30-second tones, a conditional stimulus (CS+) reinforced with an electrical shock lasting 1 second and a discriminative stimulus that was not reinforced. The presentation of the CS+ evoked significant ($n = 9$, $p < 0.01$) increase in: (a) mean aortic pressure (13.8 ± 1.9 mm Hg); (b) left ventricular dP/dt (an index of inotropic state of the heart, 850 ± 117 mm Hg/sec); and (c) heart rate (44 ± 4 beats/min). In a similar manner, the coronary vascular response consisted of an initial coronary blood flow (CBF) decrease followed (−3.0 ± 1.1 ml/min) by a larger increase in CBF (16.6 ± 2.4 ml/min). Concurrently, coronary vascular resistance (CVR) initially increased (0.52 ± 0.18 mm Hg/ml/min), then decreased (−0.77 ± 0.12 mm Hg/ml/min).

Anterior wall myocardial ischemia was then induced by the inflation of a pneumatic occluder placed around the left anterior descending coronary artery. The cardiovascular response to the aversive stress was significantly altered by acute ischemia. In particular, significantly smaller heart rate (20.7 ± 3.8 beats/min) and CBF increases (8.6 ± 3.2 ml/min) were noted during ischemia. Furthermore, the increase in CVR (0.08 ± .10 mm Hg/ml/min) as well as the CBF (−1.6 ± 1.4 ml/min) reduction were eliminated during ischemia. The mean arterial pressure (12.4 ± 1.8 mm Hg) and left ventricular dP/dt max (650 ± 210 mm Hg/sec) response, however, were not affected by ischemia. In the absence of the aversive stress, anterior wall myocardial ischemia elicited a tachycardia and modest hypertension.

Thus, it would appear that the predication based on the response to aversive stress and ischemia alone was incorrect. The interaction of these responses was more complex than would be expected from the summation of two passive reflexes. In fact, the behavioral response was reduced rather than enhanced, as had been predicted. Indeed, the combination of a reduction in the heart rate increase and the elimination of the CBF reduction would reduce the metabolic demand placed on the cardiac tissue and may serve to "conserve" the oxygen the tissue still receives. Thus, from a teleological point of view, the reduced behavioral response noted during myocardial ischemia may be adaptive, reducing the metabolic strain placed on the already ischemic cardiac tissue.

These data, I believe, further suggest that the cardiovascular system forms an integral component of the behavioral response. The cardiovascular response is not a passive reflex that merely reacts to an adequate stimulus. Rather, it is dynamic, changing to match the needs of the current situation against the background of the functional status of the organism.

The circulation, behavior, and striate muscular activity

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Engel's article outlines the considerable progress that has been made in identifying physiological pathways by which psychological and cardiovascular processes are linked. Much is known about the structure and function of cardiovascular reflexes, and this information has been used effectively in analyzing how environmental contingencies may produce predictable changes in the circulation (e.g., Obrist 1981; Steptoe 1981). Nevertheless, as Engel points out, much remains to be learned about the processes of reflex modulation and particularly about how competitions are resolved between the many inputs that vie for access to the final common pathways of the cardiovascular system. He suggests that these processes are controlled by the central nervous system, which assesses the biological utilities of available cardiovascular options and then implements its priorities by integrating competing reflexes. It is difficult to understand how this proposal, which introduces a teleological dimension to Engel's analysis, can assist in achieving what I understand to be his purposes.

Engel makes a strong distinction between "emitted" and "elicited" cardiovascular responses. He says, "They [cardiovascular responses] not only can be elicited by adequate stimuli, they can be emitted to produce stimulation" (section 5). Although it is well established that cardiovascular responses meet the operational criteria for classification as operants, the implications of this observation for understanding the physiological mechanisms underlying cardiovascular control are as obscure today as they were when research on this topic began to expand twenty years ago. To some extent this may be because the Skinnerian concept of an operant, as an activity of unknown origin (emitted) that is influenced by its consequences, has continued to resist physiological modelling. Hence, the characterization of cardiovascular activities as operants should not be expected to carry advantages in describing the physiological mechanisms underlying psychogenic changes in cardiovascular performance.

Furthermore, it would appear that much of the variance in cardiovascular performance attributed to operant conditioning procedures may be understood in terms of the effects of these procedures on striate muscular and respiratory activities. It is well established that cardiovascular responses are closely coupled to variations in striate muscular activity through a variety of pathways. These emanate directly from receptors in the muscles themselves (Mitchell & Schmidt 1983), from central structures associated with striate muscular control (Smith 1974), and from chemoreceptors that are sensitive to changes in blood gas composition produced by striate muscular activity. In addition, autoregulatory processes that are embedded in the structure of the cardiovascular system ensure that even when the heart has been denervated performance of the circulation is closely attuned to the perfusion requirements of striate muscle activity.

That striate muscular processes, operating through known reflex pathways, underlie operant cardiovascular effects is suggested by a number of experiments. For example, Brener, Phillips and Connally (1977, 1980) found in rats that operantly conditioned changes in tonic heart rate were accompanied by parallel variations in oxygen consumption ($\dot{V}O_2$). These changes in metabolic rate, which were of a far greater magnitude than could be accounted for by the metabolic costs of the observed changes in cardiovascular performance, were accompanied by correlated variations in striate muscular activity. In the 1980 study no differences in heart rate, $\dot{V}O_2$, or ambulation rate were found in a comparison of two groups of animals, one of which was reinforced for increases in heart rate and the other of which was reinforced for increases in ambulation rate. This suggests that the nervous system interprets experimental requirements for cardiac variations as requirements for striate muscular activity. A similar conclusion is supported by several studies that examined transfer of operant heart rate control between curarized and noncurarized states (Black 1967; Dicara & Miller 1969; Goesling & Brener 1972).

In making the case that cardiovascular control processes are sensitive to the Law of Effect, Engel draws on experiments in

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which biofeedback procedures have been used to modify the cardiovascular responses elicited by exercise. However, here again, there is no evidence that the reflexively controlled perfusion functions of the circulation have been influenced by the Law of Effect. For example, in a Perski, Tzankoff, and Engel (1985) experiment, reductions in heart rate during dynamic exercise were accompanied by parallel reductions in pulmonary ventilation and $\dot{V}O_2$. This suggests that when subjects reduced their heart rates, they reduced activity in muscles that were not implicated in the exercise. The same explanation can account for Carroll and McGovern's (1983) observation that although subjects could elevate their heart rates above levels elicited by isometric muscular exercises, the increases in heart rate were accompanied by parallel increases in ventilation and $\dot{V}O_2$. Similarly, we (Moses, Clemens & Brener 1986) have found that although subjects were able to increase and decrease their heart rate responses to an isometric exercise challenge, the cardiac changes were accompanied by parallel changes in ventilation and $\dot{V}O_2$. Furthermore in this experiment it was found that subjects who were not provided with exteroceptive feedback contingent on heart rate variations (biofeedback) were just as successful in modifying their exercise-related heart rate responses as were subjects who received biofeedback.

Engel's claim that cardiovascular activity is an essential component of behavior is indisputable. However, his suggestion that variations in cardiovascular performance may be behavior in the same sense that striate muscular activity is behavior seems unwarrantable and of limited utility in promoting a physiologically based understanding of how psychological and cardiovascular processes are linked. Sherrington (1940) recognized that even the most simple anatomical structures are purposive in that their adaptive functions have permitted them to survive the processes of natural selection. In this vein, it seems more plausible to propose that the priorities among cardiovascular adjustments are set by similarly selected hard-wired structures than by on-line cost-benefit analyses.

Extension of proposed concepts of cardiovascular behavior from normal to abnormal function

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The experiments reported by Dr. Engel convincingly demonstrate that cardiovascular behavior is conditional upon environmental factors. The concepts developed from the results of these experiments are not only relevant to normal cardiovascular function but also necessary for an understanding of cardiovascular dysfunction. Environmental situations that induce cardiovascular dysfunction can be manipulated by behavioral variables.

We have recently reviewed some of our own research that provides examples of changes in cardiovascular dysfunction with behavioral manipulations (Corley 1985). As an extension of findings that pathological changes were induced by exposure to unsignaled-shock avoidance paradigms, a similar paradigm was used to study cardiovascular function. Squirrel monkeys exposed to this unsignaled-shock avoidance paradigm exhibited two types of cardiovascular pathology and dysfunction (Corley, Shiel, Mauck & Greenhoot 1973). First, cardiomyopathy was observed that was similar to myocardial changes associated with abnormal enhanced sympathetic activity. Second, arrhythmias with profound bradycardia and cardiac arrest were evident. Study of these phenomena revealed that the occurrence of myopathy and arrhythmias could be modified by the manipulation of coping behavior.

Yoked pairs of monkeys were exposed to the shock paradigm. An avoidance animal in each pair had access to a lever and had the opportunity to control shock presentation. Its yoked partner, however, was subjected to all aspects of the experiment and shock but had no opportunity to influence shock occurrence. Myocardial dysfunction and pathology were explored in two experimental variations where the preparation of the animals before the exposure to the shock paradigm was manipulated.

The monkeys in the first experimental variation were exposed to the shock paradigm in 1-hour sessions until the avoidance monkey had a well-established avoidance behavior. Then sessions of 8 hours "on" were alternated with 8 hours "off" the shock paradigm (Corley, Mauck & Shiel 1975). While no differences between 6 yoked pairs were evident in cardiomyopathy, bradycardia and cardiac arrest, with no apparent cardiac distress of the partner, occurred in 5 yoked and only 1 avoidance monkey. The second experiment subjected 11 yoked pairs of animals to a single 24-hour period of the same shock paradigm, but the monkeys had no previous exposure to the shock (Corley, Shiel, Mauck, Clark & Barber 1977; Corley, Mauck, Shiel, Barber, Clark & Blocher 1979). Thus, the avoidance monkeys were required to cope with the unsignaled-shock avoidance paradigm without prior experience. While myofibrillar degeneration was evident in both avoidance and yoked monkeys, 8 avoidance animals had more of this pathological change than their yoked partners. Whereas myofibrillar degeneration in the other pairs was equal, the myopathy was more extensive in avoidance monkeys. Although fewer cardiac arrests occurred, 3 out of 4 of these arrhythmias were observed in avoidance monkeys.

Although myopathy and dysfunction were observed in both avoidance and yoked situations, these data suggest that the occurrence of the cardiomyopathy and arrhythmias can be modified by manipulation of coping behavior. Cardiomyopathy became more pronounced in the avoidance situation when the coping requirements of the first experiment were made more difficult in the second experiment. Arrhythmias occurred most often in the yoked situation, with absence of coping behavior as shown by the first experiment, but when coping in the avoidance situation was made more difficult in the second experiment, cardiac arrest was observed in the avoidance situation. Thus, arrhythmias occurred most often in monkeys with reduced opportunity to cope with the shock situation. Therefore, the important point is that the occurrence of these phenomena was modified by manipulation of the behavioral variables related to coping experience with the shock. These differences are best explained if the cardiovascular system does not have an invariant response to shock but rather interacts with environmental stimuli, as Engel has proposed.

Central command and reflex regulation: Cardiovascular patterns during behavior

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Every specific behavior (even if in real life the term "specific behavior" is only approximate) is accompanied by cardiovascular changes. These changes are characteristic of that behavior, are initiated in the central nervous system and are variously affected by reflexes carrying feedback information from the periphery. This is how most physiologists view behaviorally linked cardiovascular patterns.

In his target article Engel reports some results from his own beautiful studies and from studies by other investigators. He attempts to show the reader that the central nervous system, acting in the context of information accumulated at a certain

time, is solely responsible for producing not only a given behavior but also its accompanying cardiovascular changes. This seems to imply that there is not necessarily a constant cardiovascular pattern for a specific behavior but that in different subjects the central nervous system may induce different and even opposite cardiovascular changes in response to the same external stimulus, if the subjects had different previous experiences.

We would like to mention two recent studies performed in our laboratory that appear inconsistent with Engel's conclusion in its more extreme implications. The cardiovascular changes accompanying fighting in the cat were studied before and after acute or chronic sinoaortic denervation (Baccelli, Albertini, Del Bo, Mancia & Zanchetti 1981). Sinoaortic denervation exaggerated the fall in heart rate, cardiac output, and blood pressure during immobile confrontation. After sinoaortic denervation, fighting caused a less pronounced tachycardia, a less conspicuous increase in cardiac output, a fall instead of a rise in blood pressure; mesenteric vasoconstriction was reduced although vasodilation in exercising hind limb muscles was not impaired. It is clear from this study that the cardiovascular pattern accompanying defense behavior is not just fully encoded and organized in the central nervous system; in order to express itself in real life it requires the support of baroceptive reflexes from the sinoaortic areas. The contribution of these reflexes is not simply superimposed upon the central pattern; it is itself modulated by the central nervous system, the reflexes being inhibited during the emotional behaviors we have studied.

In a more recent study (Del Bo, Baccelli, Cellina, Fea, Ferrari & Zanchetti 1985) we considered a wider repertoire of behaviors and found that the problem is even more complex, but the central commands and the reflexes are still both at work and strictly integrated during the various behaviors: in particular, the modulation of carotid sinus reflexes during emotional behavior may be a dynamic phenomenon, with an inhibition occurring at the very beginning of fighting and then decreasing afterwards, so that the reflex response does not seem to be affected by the behavior when tested during prolonged emotional behavior. Furthermore, desynchronized sleep has been found to be accompanied by unique changes in the reflex responses of heart rate and blood pressure to manipulation of the carotid sinus receptors: the reflex responses to carotid sinus stimulation were preserved while the reflex responses to carotid sinus deactivation, both of heart rate and of blood pressure, were found reduced in comparison to quiet wakefulness.

Both studies confirm what was shown by several investigators working with the anesthetized animal, namely, that reflex cardiovascular responses (like the somatic reflexes) are modulated by the central nervous system. What the studies of freely moving animals add is that this modulation is complex, different in different species, different in different behaviors, and possibly different at different times during the performance of the same behavior. Our proposition at the beginning of this commentary needs to be worked out in more detail and more information is needed about the ways central and reflex contributions are integrated in producing the cardiovascular patterns occurring during everyday life. We believe, however, that both actors, the central command and the reflex feedback, are always on stage.

Is circulation a conditional operant or has a behaviorist discovered cognitive structures?

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Dr. Engel has mounted an impressive attack on the psychology of the 1930s and the interpretation of nineteenth-century physiology on which it is based. The attack, however, is less impressive relative to current physiological views and information processing theories of psychological functioning. Indeed, the conclusion that cardiovascular adjustments are components of cybernetic structures producing purposive behavior seems to follow from his arguments at least as well as does his view that such adjustments are classical and operant responses.

The basic points of the argument are well taken and well illustrated. Reflexes cannot be thought of as static responses, but rather as response organizations that are "integrated components of behavioral acts" (Section 4) influenced by the goals of the organism. The modifiability of reflexes is currently proving to be an important tool for analyzing information processing requirements of tasks (e.g., Graham 1984). Furthermore, cardiovascular adjustments can be proactive. In addition to Engel's elegant demonstration, anticipatory adjustment of the cardiovascular system in support of anticipated actions has been demonstrated (e.g., Jennings, 1982). Finally, I can also corroborate the finding of partial independence of cardiovascular adjustments from oxygen requirements and the multiplicity of their central nervous system sites of control.

What views are being questioned by these excellent arguments? Two alternate mechanisms of response integration are suggested by Engel: first, a prewired system in which certain reflexes are dominant regardless of conditions and, second, a system in which the cardiovascular adjustments are "determined by the situation and by prior experience." Given the adaptability of life forms, the choice between these seems clear. Few physiologists would opt for the telephone-exchange reflex model (e.g., Brooks, Koizumi & Sato 1979). Indeed, based on current knowledge, the baroreceptor reflex used in Engel's examples is less like a stereotyped response to a fixed stimulus than a control system with input and output adjustments based on negative feedback and modulation of the set point by input outside the "reflex." If Engel's first option is a "strawman," the discussion must center on the balance between inherent organization of the neural control of the cardiovascular system and its adaptability to external conditions.

Given this rephrasing of the problem, Engel's argument becomes somewhat unclear. The structured nature of the cardiovascular system and its control is recognized, but it is not clear that conditioning techniques are able to completely rewrite these blueprints. How exactly do conditions and history interact with cardiovascular control systems? Equally important is the question of how much structure in the central nervous system Engel recognizes. Does it possess internal structures determining the perception of the world and organization of responses to it; or is it an infinitely malleable organ system? A response is said to acquire "abilities to interact directly with the environment," but the nature of that ability is not discussed.

The points raised by Engel are reminiscent of those raised by early cognitive theorists (e.g., Tolman) against reflex-based theories (e.g., Hull's). Does a rat chain together specific motor responses to learn a maze or did it learn a plan that could be executed with any motor response? Can a rat act on the basis of anticipation or expectancy or only react to stimuli? Engel seems to opt for expectancy and plans when he suggests that "the cardiovascular system can be said to have a role in purposive behavior comparable to that ascribed to the somatomotor system" (Section 4). Much of the rest of his discussion, however, emphasizes classical and operant associations rather than cognitive structures.

Given the points raised by Engel, I'd not go back as far as Sherrington to find a useful conceptual framework, but only as far as early communication theory. Perhaps Miller, Galanter, and Pribram's (1960) influential introduction of these concepts into physiological psychology might do. The baroreceptor reflexes and even motor "reflexes" are described reasonably well (albeit somewhat simplistically) by the cybernetic system in which input is processed and output is adjusted relative to an

internal setpoint or image. This "reflex" structure is then embedded hierarchically in other cybernetic structures that can act on the setpoint or image of structures lower in the hierarchy. A plan or "purposive behavior" (to use Engel's term) can optimize such a system's activity by changing the setpoints throughout the hierarchy. Although simplistic, such a view leads us toward identifying the variables that are regulated, the variables that serve as setpoints, and then toward the factors controlling the aspects of the system that can be altered. This seems more in line with Engel's arguments than the psychological concepts he offers in his article. [See also Toates: "Homeostasis and Drinking" *BBS* 2(1) 1979.]

Exactly how are cardiovascular adjustments integrated with the processing of information and subsequent action? This remains a more important issue than Engel's current theoretical stance. From an information processing perspective, Sanders (1983) has raised the similar issue of how "energetic" aspects of the organism are integrated with information processing. A forthcoming volume by Hockey, Gaillard and Coles (in preparation) deals in some depth with the issue. From my own perspective, solid investigations like Engel's are needed to challenge the rigidity of what seem to be structural relations. Given our knowledge of the structure of cardiovascular control, such studies may be particularly useful in sharpening our ideas about the interaction of structure and adaptability in physiology and behavior.

Cardiovascular adjustments are a part of behavior

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As Engel concludes, the responses of the cardiovascular system to stress, including exercise, are complex but not reflexive in nature, and are sensitive to the prevailing environmental circumstances. The pertinent scientific demonstrations in the case of exercise spanned a period of at least a half century. Ernest Starling (1918), using data obtained from his isolated heart-lung preparation, attempted to explain the cardiac adjustments seen in exercise. At the start of exercise, he claimed, blood would be forced from the active muscles to the heart, thereby overfilling it. This would result in a greater stroke volume and hence the greater cardiac output required in exercise – an entirely reactive view of the operation of the circulation in exercise. Yandel Henderson (1923) took the position that changes in cardiac output needed in exercise were achieved primarily as the result of changes in heart rate mediated by the autonomic nervous system. Sarnoff and Berglund (1954) demonstrated that the response of the heart to filling depended on its physiologic state, which could be modified by procedures such as the injection of epinephrine. Smith, Rushmer, and Lasher, in 1960, reported results of studies in which they electrically stimulated the fields of Forel in the diencephalon and demonstrated that many of the cardiovascular adjustments seen in exercise took place before any exercise was undertaken. Then, in 1962, Sonnenblick described the force-velocity relations in heart muscle showing that the catecholamines exerted a marked effect on the ability of the heart muscle to increase energy delivery during contraction. Cardiac function is now clearly recognized as being under the control of the autonomic nervous system in exercise as well as in other stress situations. Stone, Dormer, Foreman, Theis, and Blair (1985) reviewed the neural regulation of the cardiovascular system during exercise and concluded that final adjustments are the result of neural integration of data from peripheral receptors, the cerebellum, and the cerebral cortex.

The catecholamines not only play a role in the immediate cardiovascular responses to stress but, under chronic stressful circumstances, they also lead to structural adaptation of cardiac and vascular smooth muscle. Folkow, in 1984, reviewed developing vascular structural adaptation as seen in hypertension. This structural adaptation progressively increases vascular resistance. The result is an upward setting of the control mechanisms responsible for maintaining blood pressure. Bevan (1984) described the trophic responses of vascular smooth muscle to norepinephrine and has described the metabolic processes concerned. Tomanek, Bhatnagar, Schmid, and Brody (1982) implicate the catecholamines in the disproportionate growth of myofibrils seen in heart muscle of hypertensive subjects. Normotension results primarily from a balance that is struck between vascular structural adaptation as described by Folkow and the availability of the catecholamines to vascular structures.

As in the case of plasma levels of steroid hormones, there is a diurnal variation of the plasma levels of the catecholamines. The observations of Raftery and Millar-Craig (1979) are a dramatic example of this as expressed in the diurnal variation of arterial blood pressure. Arterial pressure is lowest in the early morning hours. It starts to rise before the individual is aroused and achieves its highest values in the late morning. It then falls throughout the late afternoon and evening. Hypertensives as well as normotensives exhibit the same phenomenon, with the exception that the hypertensives have higher values throughout the twenty-four-hour period. Heart rate follows precisely the same cycle.

The circulatory system can respond differently to standardized stresses at different times of the day. Reiley, Robinson, and Minors (1984) reported a circadian rhythm in the heart rate response to a standardized exercise. A more complicated adjustment involving the cardiovascular and renal responses to central volume expansion was found to be suppressed in man at night by Krishna and Danovitch (1983). This is a complex adjustment involving cardiac neural receptors as well as both neural and humoral effector mechanisms. It is an adjustment that may be related to positional changes while sleeping.

In addition to the diurnal periodicity of the neurohumoral mechanisms affecting the cardiovascular system, acute events can cause large displacements from resting values. Plasma levels of catecholamines can be large in severe exercise. They are metabolized rapidly under such circumstances, however, and tissue concentrations are held to low values. Events triggering a flight-fight response without vigorous physical response can, on the other hand, result in significant increases in tissue levels of the catecholamines. As noted above, such increases in the tissue levels of these hormones may lead to structural changes in cardiovascular tissues.

While most of the discussion here has focused on the catecholamines, steroid hormones are an equally important part of the behavioral response to stress. Figure 1 is a conceptual presentation of how the two hormonal systems interact in the course of normal activities of the individual. There is a healthy operating region that accounts for the diurnal as well as acute variations of short duration of both the catechols and the steroid hormones. The recognition of the importance of the link between behavior and the production of the two hormonal moieties is a necessary step toward understanding the potential for developing both functional and anatomical pathology.

The reflex remains

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Engel marshals his impressive corpus of work to make the point that cardiovascular "reflexes" are like any other "behavior" in

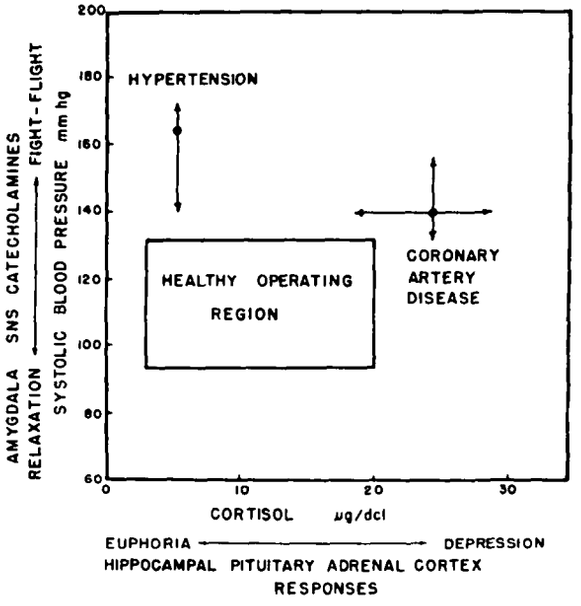

Figure 1 (Meehan). Graphic representation of the interaction of the two main stress response systems. SNS = sympathetic nervous system.

being able to fall under stimulus control. Many of my own experiments likewise support the notion that cardiovascular change can be more than reactive. But rather than throw out the baby with the bath water, I would like to argue for the primacy of the reflex and for the need to fill in many blanks before we can be sure that cardiovascular "behavior" is identical to skeletal motor "behavior."

It was probably the development of the conditional emotional response that caused Pavlovians in this country to stop studying visceral respondents and turn instead to skeletal motor responses, i.e., suppression of lever pressing. The decision to do this was probably technical. By studying lever pressing behavior, the psychologist would be able to get at the principles of behavior more easily than by instrumentation of visceral systems. That strategic turn, however, which was fabulously successful in the hands of modern Pavlovians such as Rescorla (1968), has made Engel's present target article necessary. The question is: If we were to repeat all the work done in the past decade using lever pressing suppression as a dependent variable but using some cardiovascular variable instead, would we get the same results? I believe Engel's hypothesis would be supported but that there also exist differences between skeletal and smooth muscle/endocrine "behavior" that might make it hard to establish his hypothesis definitively. For me, the importance of Engel's contribution is in refocusing attention on visceral conditioning. To confirm his hypothesis will require more experiments. Just as research in Pavlovian conditioning of motor behavior can produce disrupted behavior (Rescorla 1968), it can produce large and sometimes sustained increases in visceral tone (e.g., Natelson & McCarty 1980). Hence, whether or not these new experiments demonstrate that visceral and motor behavior are alike or somehow different, they will help us understand the states of visceral and behavioral arousal characteristic of clinical syndromes such as the posttraumatic stress syndrome. This research may teach us something about disease as well as about behavior.

Let me be more specific. If heart rate comes under stimulus control or is conditional in the same way as lever pressing behavior, one would expect the visceral variable to follow the same set of rules as the motor behavior. Extinction is one such test. After removal of the unconditional shock stimulus, the animal's appetitive lever pressing behavior during the conditional stimulus slowly returns to baseline – thus displaying extinction of the conditioned suppression or the conditioned emotional response. This can happen in dogs, but Gantt (1960) makes the point that for "many animals extinction of the cardiac conditional reflex is impossible." Similarly, Caul and Miller (1968) did not find monotonic changes in resistance to extinction of the heart rate response as the informational value of the signal preceding the shock was degraded. In these examples, the animal fell either too greatly or not enough under the influence of the experimental stimuli. One of several possible explanations of the differences between the visceral and skeletal respondents is that they are classes of respondents. In contrast to motor behavior, heart rate is very slow to habituate to novel stimuli (Snapper, Ferraro, Schoenfeld & Locke 1965). It may be energetically cheaper for the animal to respond than not to respond to a stimulus that is no longer salient. Obviously, additional parametric experiments would resolve this question and determine whether an important class difference really exists or whether the question is merely one of degree.

Having made this cautionary observation, I will now turn to the evidence that the cardiovascular system can fall tightly under stimulus control. To supplement the references cited in Engel's target article, I would like to describe some data collected in my laboratory. In addition to the well-described changes in heart rate during classical conditional stimuli, heart rate also follows contextual cues. Thus, in an experiment where dogs were subjected to signaled shock in one context and to signal alone in a different context, basal heart rate prior to the delivery of the first signal was significantly higher in the context where shock was delivered than in the control context (Creighton, Natelson, Ferrara, Cook, Curtis & Tapp 1983). Similarly, Anderson and Brady (1971) have noted that chronically instrumented dogs show anticipatory changes in cardiovascular parameters that begin to occur at least an hour before the session starts. These contextual, conditional changes look like giant fixed-interval scallops and closely resemble lever pressing behavior in anticipation of single daily access to food.

We have also shown that health consequences occur when the cardiovascular system falls under experimental control. We have studied the ventricular arrhythmias that occur in subjects when too much cardiac glycoside (i.e., digitalis) is administered (see Natelson 1983 for detailed review). These drugs are commonly administered to patients with heart disease, many of whom develop life-threatening cardiotoxicity. Unfortunately, whether a patient develops such toxicity is not highly predictable from blood levels of the drug. One of the reasons for this is that other blood-borne factors such as ion and hormone concentration can predispose one to this condition. We hypothesized that environmental factors also could do this. In a series of experiments, we showed that acute stress precipitated digitalis toxicity and that this effect habituated with repeated presentation of the stressor. We then showed that arrhythmia onset was conditional on the context in which the drug was administered. In one set of experiments we found that arrhythmia onset occurred significantly more often during a signal previously paired with shock than with the signal alone, and, in other work, that the time it took to develop these digitalis-induced arrhythmias was significantly shorter when the drug was given in an environment where signalled shock but not the signal alone had previously been delivered. Because conditional changes in heart rate have been so commonly reported, we had hypothesized that they might be correlated with the context-bound sensitization we had found. However, in another experiment in which we monitored heart rate in our experimental animals (guinea pigs), we did not find conditional changes in heart rate. Although other experiments have made it clear that the sensitization has a cholinergic mechanism, we currently do not know exactly what cardiovascular variable is

being conditioned and is responsible for the sensitization seen in our experiments. A final point: In contrast to these negative results in the free-ranging guinea pig, we did find definite stimulus-bound heart-rate slowing in restrained guinea pigs. This is another example of Engel's point that a conditional reflex can be affected by the context in which the conditioning occurs.

The validity of Engel's suggestion that physiological reflexes such as the diving reflex can be shown to be conditional seems arguable, at least to a degree. Kanwisher et al. (1981) reported that the diving reflex was robust when ducks were forced to dive but trivial or nonexistent in birds with experience in diving. They concluded that emotional stress was chiefly responsible and suggested that diving was relatively unimportant. This conclusion was surprising in view of the fact that diving-related bradycardia occurs in freely diving seals (Kooyman & Campbell 1972) and humans (Hong, Song, Kim & Suh 1967) and also occurs when chronically decerebrated cats are submerged or undergo nasal injections of water (Martner, Wadenvik & Lisander 1977). When I was a subject in such an experiment, the diving reflex occurred reliably and repeatedly, and I did not feel at all stressed (Kawakami, Natelson & DuBois 1967).

I and my colleagues consequently examined the effects of anoxia and water temperature on face-immersion-induced bradycardia in human volunteers (Natelson, Nary, Curtis & Creighton 1983). Concurrent with face immersion, we asked the volunteers to rate the degree of stress they were experiencing. We found that the magnitude of the elicited bradycardia depended most on water temperature, with apnea playing a less important role. Perceived stress did affect the magnitude of the response, but this was less important than the other variables. Ross and Steptoe (1980) have similarly shown that distracting the subject by having him perform mental arithmetic lessens the magnitude of the bradycardia, although the combined effect of holding one's breath together with face immersion was prepotent. The results of these studies – that arousal or stress diminishes the diving reflex – is opposite to the conclusion of Kanwisher et al. (1981).

That animals have a profound reflex "fright" bradycardia cannot be denied. But our data make it clear that face-immersion-induced bradycardia cannot be dismissed as an artifact of emotional arousal. The diving reflex is indeed a reflex induced by facial immersion in cold water, although it can be modified by environmental factors. But here the degree to which the reflex can be brought under stimulus control is important. For mild to moderate environmental disruption, the reflex change still occurs; whether more marked stress would abolish the reflex altogether or elicit the fear-related reflex is a matter for speculation.

The important point is that the occurrence of reflexes such as this one is not so conditional as to make it useless to consider in and of itself. My conclusion is that the reflex occurs and is in fact prepotent, but that it is modifiable by environmental inputs. This is not so different from the case of the tendon reflexes used clinically by neurologists. When the tendon is tapped, a muscle jerk occurs. But this motor reflex is far from constant. Environmental stimuli and the activation of supraspinal neural activity can modify the intensity of the elicited response. The more relevant point is that usually the reflex does occur. Thus, were Lord Brain alive today, he would argue that there is still a great deal to teach and study about the reflex – be it of brainstem origin, as the diving reflex is, or more complex, as with fear-induced bradycardia. I would certainly agree both with Brain and with Engel, however, that these reflexes, whether of striated or smooth muscle, cannot be viewed *in vacuo*, but must, like any other respondent, be considered susceptible to environmental influences and external control.

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Evidence for instrumental plasticity in the cardiovascular system is circumstantial

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Engel proposes that cardiovascular responses are organized into functional acts by an instrumental process comparable to that which guides the activities of the somatomotor system. I describe some conceptual concerns and offer a different assessment of existing evidence.

The motor system (including perceptual processing) is the system by which organisms interact with an environment whose demands and particular features are unique to each member of the species. On the basis of previous experience, information about the present state of the effectors, and the goal to be achieved, a movement is computed and executed. However, if the topography of goal-relevant behavior cannot be retrieved from memory (as is true for the untrained organism) or inferred from the task environment (as in the case of ambiguous task situations), exteroceptive feedback from the environment indicating which actions are relevant to success is necessary. Engel's biofeedback experiments present the organism with problems of this type. Because the motor system is specialized for dealing with organism-environment interactions, we would expect this sytem to be engaged. Information will accumulate about patterns of motor behavior related to feedback, which in this case will be motor patterns associated with cardiovascular adjustments appropriate for the prevailing feedback contingency.

Unlike the motor system, the cardiovascular system operates in a milieu that is highly similar for all members of the species. One might expect this uniformity to favor a system designed to monitor and react to disturbances in internal state through intrinsic mechanisms, and to support the metabolic demands of somatomotor and other activities through neuroanatomical integration within these systems. In addition, the cardiovascular responses required to maintain the internal milieu appear similar enough across situations and conspecifics to diminish the necessity to learn about these responses from a monitoring of their consequences, as is required in the case of the motor system, which mediates more variable organism-environment interactions. Thus one can ask why the cardiovascular system should learn from exteroceptive feedback to the same degree the somatomotor system does, or, for that matter, why it should learn from exteroceptive feedback at all. Engel might not, of course, intend a thesis of parity. For example, he might intend to suggest that learning through exteroceptive feedback is merely a factor in cardiovascular organization, or that cardiovascular adjustments are learned through their ability to correct internal metabolic disturbances. The latter idea has been a driving force in research on visceral learning for more than a decade, although evidence for operant autonomic learning as a mechanism of homeostasis is problematic (Dworkin 1984; Roberts 1978).

Of course, these conceptual reasons for caution might be reversed by new evidence. Has Engel provided this? I don't think so, at least not yet. Of greatest relevance is his preliminary report that an exercise contingency was complied with more efficiently when a decrease in heart rate was simultaneously trained than when heart rate was uncontrolled. The implication is that the animal has retained information about a specific cardiovascular adjustment under the combined contingency. However, in the absence of further details regarding baseline

performance, training procedures, the composition of cardiovascular state, and what the monkeys actually did, it is difficult to assess alternative explanations. Engel's exercise contingency notwithstanding, it is possible that the pattern of motor behavior exhibited by the monkey differed between the exercise-alone and combined conditions, and that the exercise-alone pattern was accompanied by an increase in sympathetic arousal that eventuated in less efficient energy utilization under this condition. Sympathetic activation might have been triggered by exercise level (Robinson, Epstein, Beiser & Braunwald 1966) or released by behavioral contrast that could conceivably have been induced by the procedures of this study (single versus dual contingency) (Mackintosh 1974). Or, grouping of the exercise-alone sessions early in the study could have confounded habituation with training conditions. On the other hand, because the results are presented as changes from an unreported baseline, we cannot assess the alternate possibility that sympathetic drive might have been elevated throughout sessions using the combined contingency. This possibility exists because such training was more demanding and probably associated more often with shock than performance under other schedules, and because the conditions signalling this type of session were apparently present during the baseline period (Ainslie & Engel 1974). Sympathetic activation elicited by the task environment could have diminished the relation between changes in heart rate and oxygen consumption by elevating the prevailing heart rate and diminishing variability in the heart rate measure. These and other possible explanations need to be looked at because intrinsic mechanisms would be expected to oppose a diminished cardiac output in the combined condition when workload is held constant. Engel's interpretation implies that cardiospecific instrumental learning is powerful enough to counteract such mechanisms, but previous efforts to uncouple cardiovascular and somatic activities through biofeedback do not encourage optimism on this point (Brener 1983; Newlin & Levenson 1978; Roberts 1978).

Having said this, it should be noted that Engel's research on instrumental learning is unique for the length of training given. Conscious processing of action-outcome relations appears important in the early stages of visceral learning (Hughes & Roberts 1985), but how information accumulates with extended training is uncertain. I look forward to Engel's experimental reports with interest.

On the circulation as cognition

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Engel makes a strong case that modifications of an organism's circulatory status is an integral part of its behavioral system. The circulation is not merely reactive, it can also be anticipatory and adaptively conditional in response to available information. Assuming that Engel is right, this claim has important implications for cognitive science. My intention here is to reflect on the impact of the circulation's anticipatory adaptive features on our notions of cognition.

A number of individuals have thought it useful (or even critical) to distinguish cognitive from noncognitive behaviors (e.g., Pylyshyn 1984; Terrace 1982; cf. Roitblat 1982; Roitblat & Weisman 1986). Noncognitive behaviors were thought to be mediated by reflex or reflexlike systems on a fairly simple mechanistic basis. In contrast, cognitive behaviors were thought to be mediated by computational systems that operated on symbolic representations in a content-dependent manner. In particular, Pylyshyn (e.g., 1980; 1984) proposed a criterion of "cognitive penetrability" to distinguish between cognitive behavior and behavior governed by "functional architecture." Behaviors that can be explained only if we know the content of the information encoded are cognitive behaviors, whereas behaviors that can be explained directly in terms of the structure of the organism, its functional architecture, or how it is "wired," are noncognitive behaviors. Cognitive behavior is modified in rational ways by information-bearing modulating events, but noncognitive behaviors bear a fixed stimulus-response relationship that is uniform whatever content or meaning the stimuli might have. "If we can set up situations demonstrating that certain stimulus-response regularities can be altered in ways that follow these rational principles, we say that the input-output function in question is cognitively penetrable, concluding that at least some part of this function cannot be explained directly in terms of properties of the functional architecture; that is, not 'wired in' but requires a cognitive, or computational, or representation-governed explanation" (p. xvii). The circulation seems to meet this criterion of cognitive penetrability. At least some part of the circulatory function is, therefore, cognitively based.

For example, animals can proactively modify their heart rates in anticipation of a signal (e.g., Gottlieb & Engel 1979; Engel & Joseph 1982). What is perhaps more important, however, is that these same animals can modify their heart rates in opposite directions in the presence of the same signal, depending on the contingencies of reinforcement. Their responses are thus seen to be rational and conditional on information-bearing modulating events. Furthermore, humans show an attenuated ability to adjust their blood pressures while performing mental arithmetic (Brooks et al. 1978), indicating that the baro-adjusting response requires mental work effort or access to some of the same resources that are necessary to perform mental arithmetic.

A few years ago I argued that no principled basis was available for distinguishing between cognitive and noncognitive functions (Roitblat 1982). The apparent cognitive penetrability of the circulation system supports this claim. The brain can be nothing more than the changing patterns of neural activity and all information, whether about the danger of a situation or the status of one's blood pressure must somehow be encoded in terms of the location and/or rate of firing of neurons. What we typically think of as cognition emerges out of the organization and pattern of these firings, but there is no principled way to distinguish between those patterns that are cognitive and those that are not.

On an a priori basis, few functions of the body seem more biological and less cognitive than the functions of the circulatory system. If the criterion fails in excluding such a biological function as the circulation, it can hardly succeed in any interesting or useful manner. Even the circulatory system is controlled by representations and computational functions that are at least similar to those that control other cognitive functions.

Circulation as consciousness

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Latent in Sherrington's (1973) concept of the reflexes is the stipulation of their dissociability. Nevertheless, perhaps due to the forceful analysis of Cannon (1929), the idea that centrally controlled reflexes responded additively remained popular. Even though popular, this idea is not as prevalent today as it was 10 years ago. Indeed, in another time, Engel's essay would have been viewed as heretical. Perhaps even today, among some groups, the idea that physiological response systems are behavior and that they are dissociable (just as walking and talking at

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the same time are dissociable) remains untenable. And perhaps there are conditions in which Engel's analysis fails. However, my comments are intended to push the issue further, to consciousness. Perhaps the pattern of "reflexes" reflects and even directs experience. Perhaps changes in the circulation and the many permutations of dissociations are experience. Of course, this view owes its debt to the mentalistic reasoning of William James (1892), and its contemporary scientific extension to the Laceys (1974; 1959; 1967; 1970). The following brief review, coupled with the analysis of Engel, supports the cardiovascular role in consciousness.

Pressure sensitive receptors (baroreceptors) in the carotid sinus and aortic arch assist in homeostatic control of blood pressure. Baroreceptors increase their firing rates during transient blood pressure increases and decrease their rate as blood pressure falls. However, the baroreceptors have functions in addition to those classified as homeostatic. In 1929, Tournade and Malmejac found that stimulation of the carotid sinus nerve diminished muscle tone in anesthetized animals. Similarly, Koch (1932) found that increased pressure in the carotid sinus of a dog led to decreased motor activity and even prolonged sleep.

Bonvallet, Dell & Hiebel (1954) discovered that increased carotid pressure shifted electrocortical activity from low-voltage fast activity to high-voltage slow activity. Thus, when the baroreceptors in the wall of the carotid sinus detected increased pressure, the electrocortical activity was inhibited (an example of dissociation). Severing the vagus and glossopharyngeal nerves released the inhibitory influence.

Cells firing with a cardiac rhythm have been recorded in the medullary areas (Humphrey 1967; Smith & Pearce 1961), and coagulation in this region prolongs the effects of a stimulus. Lacey (1967) has suggested that the function of this area, rich with cardiovascular representation, may be to "control the duration of an episode of stimulus produced in the brain" (p. 27).

Evoked potentials in supramedullary areas (posterior hypothalamus) occur as early as 10 msec following stimulation of the carotid sinus (Adair & Manning 1975). When, in turn, these hypothalamic areas were stimulated, a 65% reduction in single-unit firing occurred in medullary neurons responsive to baroreceptor activation. Another supramedullary structure responsive to vasomotor activity is the locus coeruleus (LC). In a series of studies by Svensson (Svensson & Thoren 1979; Persson & Svensson 1981), blood was withdrawn (experimental hemorrhage) or fresh blood loaded into conscious rats. After blood loading (increased pressure) behavioral depression and inhibition of NE (norepinephrine) and neuronal firing rate was observed in the LC. Hemorrhage resulted in increased exploration and activation of NE and neuronal firing rate in the LC. Earlier, Coleridge, Coleridge & Rosenthal (1976) found that distension of the carotid sinus caused prolonged depression of activity of pyramidal tract cells in the motor cortex. Similarly, human spinal cord excitability has been shown to vary directly with the cardiac pulse. Forster and Stone (1976) demonstrated that the "physiological tremor" of normal skeletal muscles was a function of cardiovascular modulation, presumably via gamma-motor neurons. They speculated that the rising phase of systolic pressure might alter neuronal excitability by a piezo-electric effect on motor neuron membrane, or that neuronal firing rate was a function of microcirculatory, oxygen-carbon dioxide tension during the cardiac cycle.

An interesting problem is the extent to which "consciousness" may be coupled with circulatory logistics. For example, Thompson and Barnes (1979) and Thompson, Yates, Franzen & Wald (1983) have mapped rapidly responding venous afferents from femoral and brachial veins to the motor-sensory cortex of cats. Stimulation of forelimb and hindlimb venous afferents resulted in unique topographic distribution of the cortical evoked response. Where stimulation was applied in the circulatory system determined the cortical response. Thus, the circulation does not send simple, additive transmissions.

In addition to the physiological relationships described, the Laceys and others (Lacey 1959; 1967; Lacey, Kagan, Lacey & Moss 1964; Sandman, McCanne, Kaiser & Diamond 1977; Sandman & Berka 1982; Libby, Lacey & Lacey 1973; Cacioppo & Sandman 1978; Hare 1973), have indicated that transient decreases in blood pressure or heart rate improve attention, and increased heart rate facilitates cognitive elaboration. However, the relationship of the cardiovascular system to the electrical activity of the brain in human subjects has received less attention. The early report of Obrist and Bissell (1955) suggested that changes in posture compromised cerebral blood flow and were reflected in the EEG. Ingvar (1972) extended these principles and demonstrated that increased perfusion was related to increased arousal of EEG patterns. Callaway and Buchsbaum (1965) and Callaway and Layne (1964) demonstrated a synchronous relationship between the ventricular contraction of the heart and the "ascending" wave of the alpha rhythm.

In a series of studies (Walker & Sandman, 1977; 1982; Sandman et al. 1982; Sandman 1984), we have described the influence of transient changes in heart rate or pulse pressure on cortical event-related potentials (ERPs) in human subjects. In these studies we have found that during transient decreases in blood pressure, early components (i.e., 100–200 msec) of the ERP were enhanced. Furthermore, this effect was especially significant in the right hemisphere of the brain. These findings suggest that ERP components thought to be related to dimensions of consciousness covary with the cardiovascular system and are lateralized in the brain.

One conclusion implied by these findings is that a portion of environmental awareness is "hardwired." That is, inviolable relationships between the heart and brain may set limits on consciousness. There may be optimal, cyclic physiological "windows" for efficient interaction with the environment. Certainly, the data from these studies indicates that there are precise periods during the cardiac cycle when perception and the impact of stimulation are optimal.

What mechanisms could account for these findings? One possibility is that blood flow changes the conductivity of the brain. In this regard, Klivington and Galambos (1967) estimated that blood contributes 10% to the conductivity of the cortex. Another possibility is that metabolic changes increase neural efficiency. For example, Willison, DuBoulay, Paul, Russell, Thomas, Marshall, Pearson, Simon, and Wetherley-Mein (1980) reported that patients with elevated VH (venous hematocrit: increasing blood viscosity and decreasing cerebral flow) do poorly on simple tests of alertness. When the VH was lowered in these same subjects, performance improved.

A third possibility is the nature of neurogenic control of the vasculature. EVRs (evoked vascular responses), elicited by auditory stimulation in humans, were measured with the rheoencephalograph and adapted to ERP procedures (Sandman, O'Halloran & Isenhart 1984). Rapid responses were identified by statistical analysis during the diastolic but not the systolic phase. The latency of the EVR defied the time course of previously described vascular changes in response to altered metabolic activity. Thus, this response may be a neurogenically mediated vascular event in preparation for altered metabolic demand.

These possibilities fall short of the heretical views of Kennedy (1959), who proposed that synchronous brain activity was an artifact induced by the mechanical energy from the ventricular contraction of the heart (Bering 1955). This "pulse," applied to a gelatinous mass (the brain), in a limited, closed container (the skull) initiated and sustained brain activity via the cerebrospinal fluid. Consciousness, or the frequency of oscillation, was related to the "consistency" of the brain and modified by the cerebral vasculature. Thus, during attention, the brain was engorged with blood, detuning the oscillators and blocking synchronous activity. These possibilities are not

mutually exclusive, and all support the radical neo-Jamesian proposal that the sea of consciousness rides on the oscillating waves of the cardiovascular system.

Vascular components of the orienting and defensive reflexes

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Cardiovascular responses are integral components of behavior. They can arise from innate genetic factors, they can be elicited by conditional stimuli, and they can be emitted in anticipation of consequences (Barry 1984; Sokolov 1963).

Parallel recordings of digital and head plethysmograms in man reveal the existence of an OR (orienting reflex) characterized by digital vasoconstriction and head vasodilatation. This OR selectively habituates with repeated stimulation and is restored by any change in the stimulus. A DR (defensive reflex) evoked by painful stimuli is marked by nonhabituating vasoconstriction in the head and hand. The time-course of the development of a classical conditioned DR in response to paired sequences of neutral and painful stimuli is characterized by two phases: (1) the initial restoration of the OR and (2) the gradual establishment of the DR accompanied by parallel OR habituation. At the beginning of the extinction of the conditioned DR, when the painful unconditional stimulus is no longer presented, the conditioned DR is followed by an OR induced by the absence of the painful unconditional stimulus.

Anticipatory vascular responses can be observed during conditioning when the painful stimuli are presented at constant intervals. The initial index of the anticipation is a conditioned OR preceding the unconditional DR. This expectancy OR is gradually followed by a time-dependent conditioned DR and the subsequent unconditioned DR and an OR evoked by the mismatch between the expected unconditional stimulus and its omission.

The dissociation between the OR and the DR under various conditions depends on parallel channels of command neurons (Kupfermann & Weiss 1978) coding vascular components of the OR and DR by the "lable line principle."

Circulatory behavior: Historical perspective and projections for the future

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Dr. Engel's perception that the circulation, as well as other visceral functions, is an integral part of an organism's behavior is important and illuminating. Although today the concept is not widely shared by medical and behavioral scientists, it is not new. One finds it implicit in Cabanis's early nineteenth-century publication, *Rapports du physique et du morale de l'homme* (Cabanis 1975) and also in Sechenov's *Reflexes of the brain* (Sechenov 1959; first published in 1863). Sechenov was a student of Claude Bernard and teacher of Pavlov. In the 1956 edition of Webster's New Collegiate Dictionary, behavior had already been identified as "The way in which an organism, organ or substance acts, especially in response to a stimulus" (Webster 1956). The concept was further articulated in a series of publications from conferences organized by Horace Magoun and Frank Fremont-Smith and edited by Mary A. B. Brazier (Brazier 1959; 1960; 1961; 1962; 1963). In the medical literature, cardiovascular responses were described as aspects of behavior at least as early as 1970 (Wolf 1970).

Engel's contribution has been to emphasize that visceral and circulatory behaviors do not occur as separate actions but are integrated into the total behavior of the organism. He points out that the integrative process depends upon interactive rather than hierarchical central control mechanisms. This view was proposed in 1963 by Brobeck and later cogently presented and documented in a FASEB symposium by its chairman, J. W. Manning and the other participants (Manning 1980). Engel's use of the term "conditional" to express the outcome of the neural interactions parallels Sherrington's (1946) way of explaining the behavior of autonomically innervated structures as "contingent."

Engel quotes Nadel et al. (1980, pp. 1495–6) to the effect that "when regulatory systems that share common effectors are presented with extreme conditions, the controlling and integrating mechanisms must search for the optimal compromise." A vivid illustration of such an optimal compromise is available in the work of Elsner and Gooden (1970), who demonstrated that the dive reflex in man elicited by face immersion caused a reduction of the reactive hyperaemia expected after release of an occluding pressure cuff on the arm. They showed a similar predominance of peripheral vasoconstriction during vigorous underwater swimming while the breath was held over what on land would have been wide vasodilatation in the exercising muscles (Elsner, Franklin, Van Citters & Kenney 1966).

Engel cites a 1976 publication by Blix as evidence that the elicitation of the dive reflex in ducks may be conditioned. Earlier demonstrations of the effects of emotionally significant circumstances on the dive reflex in alligators had been made by Anderson (1961), in seals, Scholander (1962), in ducks, Folkow (1966), and in humans by Wolf (1964; 1965). Engel's suggestion that the cardiovascular system can have a role in purposive behavior comparable to that of the somatomotor system is refreshing; and, indeed, since there are responses in anticipation (proactive in Engel's terms), it is difficult to escape the notion. Rushmer documented cardiovascular adjustments appropriate to exercise in dogs familiar with the treadmill procedure who were standing quietly alongside the apparatus prior to running (Rushmer & Smith 1959).

The useful phylogenetic perspective Engel provides emphasizes the growing repertoire of protective patterns that can be called upon in making adjustments to one's circumstances and the increasing complexity involved in making adaptive decisions. Engel's work has shown how patterned responses in monkeys can be manipulated by long term conditioning. His experiments are ingenious, elegantly designed, precisely focused, and convincing.

Engel points out the difficulties of attempting comparable studies in humans, especially noting the severe limitation on controls, but he neglects to highlight the limitations of studies with animals who cannot communicate their thoughts and emotions and in whom one can scarcely infer the sort of cognitive and emotional factors that enter so powerfully into the integrative process that determines visceral aspects of behavior in man.

Apart from urgent priorities of cardiovascular response when survival is at stake, as noted in apnea during submersion, what Engel calls contextual factors become dominant in determining what response pattern emerges. In man these factors consist of a complex of circumstances, timing, preconceptions, beliefs, social pressures, emotionally significant past experiences, self-doubts, aspirations, and personal values. These and other intangible but powerful forces, acting through the central neural circuitry, shape the response pattern and thereby provide a severe challenge to the investigator who would pose behavioral questions to man. As discouraging as the challenge may seem, however, there are strategies to meet it, strategies designed to yield not only quantifiable data but data on configuration, that is, the arrangement of circumstances in relation to pecularities of individuals (Schottstaedt et al. 1958).

Rapid developments in neuroscience have begun to delineate the central neural circuitry and the chemical means whereby meaningful events can influence bodily processes. Nevertheless, conclusive evidence remains to be adduced through the study of intact behaving human beings. Despite the inherent difficulties, if we are to work with more than trivial indications of how a person sees his world and reacts to it, we must apply ourselves to ever-improving strategies. Today, despite the availability of a profusion of sophisticated, often noninvasive instrumentation capable of precise measurement, few investigators seize the opportunity to study living, behaving human beings.

Program control of circulatory behavior

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As indicated in Engel's target article, Sherrington and coworkers placed considerable emphasis on the control of movement by chains of reflexes (Mott & Sherrington 1895; Sherrington 1898). However, Sherrington was not a strong advocate of programmed movements, as proposed by Brown (1911), Sherrington's contemporary. A program is a series of sequential command signals to carry out a task in an integrative manner. Brown (1911) and later Shik, Severin and Orlovskii (1966) and Grillner and Zanger (1975) contended that movements are controlled by neural "programs" that could be modulated by feedback from afferents (i.e., reflexes) but were not basically driven by chains of reflexes. Like a computer program, the neural program functionally restructures the neural circuit to carry out the task.

Cardiovascular and respiratory responses to different physiological states can be thought of as a part of a neural program. Although Engel uses the term "behavior" in a similar manner, it could have different connotations. Although the term "program" implies a mechanism to produce behavior the behavior can be more a result of a program. Descriptions of behavior are an important first step in understanding the program. The term "central command" is often used in place of the nonreflex portion of the program for studies of cardiovascular and respiratory responses to physiological states such as exercise. [See Kupfermann & Weiss "The Command Neuron Concept" *BBS* 1 (1) 1978.]

The same apparent behavior (e.g., exercise) may be a part of different programs. For example, an experimental animal may run on a treadmill out of fear or joy. The programs underlying these two exercise states may be different; yet, part of their expression, the running behavior, may appear quite similar. This could explain why different results and conclusions may follow from the same externally expressed behavior in studies from different laboratories.

Baroreflex regulation of systemic blood pressure can play an important role in cardiovascular portions of these programs. I would be cautious about extrapolating blood pressure regulation from strictly reflexive heart rate changes to induced changes of blood pressure. Engel describes changes in baroreflex regulation from heart rate data; yet, under the same behavioral conditions, he reports no change in blood pressure. How can one state that the baroreflex regulation of blood pressure has changed? Obviously, the baroreflex regulates blood pressure, not heart rate. In the simplest analysis, if a blood pressure change is induced by any program (e.g., exercise), then either resetting has occurred or sensitivity has been changed. Among the exceptions to this view, in theory, would be a change in sensitivity compensated by resetting or vice versa. Another possibility would be if a blood pressure perturbation exceeded the system's ability to compensate or correct. Using the chronic isolated sinus preparation in dogs to avoid these problems, our laboratory has reported persistent, although attenuated, baroreflex control during exercise (Geis & Wurster 1980). The role of baroreflex regulation cannot be studied only through heart rate changes. Here, part of the program of exercise includes elevated blood pressure and heart rate with attenuation of baroreflex responses to increased blood pressure.

Engel discusses studies involving lesions of peripheral autonomic and central nervous system structures. For example, the lesions of cardiac nerves may indicate that cardiac innervation is important for the observed cardiac changes in a given physiological state (e.g., heart rate changes during stress). However, this does not tell us much about the central nervous system controller of the program and what information is being used. The effects of lesions of the solitary nucleus (the principal termination of baroreceptor afferent fibers) on blood pressure control during certain physiological states tell us that baroreceptors may attenuate blood pressure changes during this physiological state. Thus, baroreflexes are a part of that particular program. Spinal cord lesion studies have examined the role of somatic afferents in the control program for cardiovascular responses to ischemic exercise (Kozelka, Christy & Wurster 1982). Other studies, primarily of descending spinal pathways, have examined their role in mediating baroreflexes and their involvement in cardiovascular responses to exercise (Geis, Barratt & Wurster 1978). Smith, Astley, DeVito, Stein & Walsh (1980) have studied the effects of hypothalamic lesions on the cardiovascular expression of some programs. These lesions were found to interrupt certain cardiovascular portions of the program but not other components (e.g., muscular exercise) or other neural-mediated cardiovascular and respiratory responses. Thus, the anatomical substrate of some of these programs is beginning to be revealed using lesion studies and chronic brain recording techniques. Of course, some caution should be applied to the interpretation of any lesion studies because the lesion may have produced a different neural circuit and program. As described elsewhere (Wurster 1984), the search for the substrate of a program should take into consideration concepts such as multiple functions of a single neuron and microcircuitry, nonaction-potential neural processing, and the meshing of one program or control circuit with another.

In summary, cardiovascular and respiratory behaviors are parts of complex neural programs. These programs can directly drive outputs to effector organs and can modulate or shape the contributions of reflexes. The role of afferents may therefore be unique for each physiological state and may result in differential neural activity with different cardiovascular effectors. These programs may restructure the neural control circuits. Describing these programs and their neural substrate calls for difficult but important studies of the sort conducted by Engel and his colleagues.

Control of autonomic nervous system-mediated behaviors: exploring the limits

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Engel's target article effectively brings together research data that are, among other things, in the process of redefining traditional conceptualizations of CNS-ANS (central-nervous-system/autonomic-nervous-system) relationships. I will concentrate my remarks on three issues raised by Engel: (1) "An underlying principle . . . that, from the perspective of behavior, the distinction between, for example, somatomotor and visceral behavior is only valid in the sense that these behaviors are mediated by different anatomical and physiological struc-

tures that impose idiosyncratic constraints on their respective performances"; (2) the significance and implications of length of training, highlighted by Engel's experiments with nonhuman primates; and (3) evolutionary considerations.

Amplifying on Engel's statement concerning CNS-mediated and ANS-mediated behaviors, it is important to keep in mind that the nervous system represents, both structurally and functionally, a complex integrated network. Specifically, (a): there are preexisting neural pathways within the CNS, and interconnecting the CNS and ANS; and (b): the (genetically determined) potential of animals (especially mammals and, amongst them, especially the higher primates) to learn complex skills, including many that are not acquired "naturally" (but by special training/experimental procedures) means that the CNS – particularly, the neocortex – has the ability to modify existing relationships between its various structures and even to establish new ones. Furthermore, since there are extensive reciprocal connections between the CNS and ANS, it is scientifically sound to posit that the CNS is potentially capable of establishing functional relationships with the ANS that could lead to the acquisition of (new) complex skills involving organs innervated by autonomic fibers, including the establishment of conscious voluntary modulation of an extent and magnitude that does not occur "naturally." Indeed, it is reasoning along such lines that had led to arguments for reconceptualizing CNS-ANS relationships (e.g., Hess 1954; Gellhorn 1967; Schwartz 1974; Obrist 1976; Sandman, Walker & Berka 1982), as well as to extensive research on the control of autonomic functions and, for that matter, control of CNS functions not traditionally considered to be under voluntary control (e.g., Sterman & MacDonald 1978; Rockstroh, Elbert, Lutzenberger & Birbaumer 1984).

Given the above, and the great amount of research effort devoted in recent years to exploring voluntary control of autonomic (particularly cardiovascular) functions, the results, while documenting the attainability of some measure of control, are, nonetheless, far short of original expectations (Blanchard & Young 1973; Williamson & Blanchard 1979). As Davidson (1980) put it, for human research, "Data are accumulating for different response systems which suggest that any control gained by making a previously unconscious process conscious through external feedback, does not typically extend beyond the normal range of variation in the particular response system in question" (pp. 25–26). I believe that the answer to this lies in the second issue I will address, namely, length (as well as quality) of training, exemplified by the performance of some of Engel's monkeys and by human results (Miller & Brucker 1979; Yellin, 1984a; 1985; Cohen & Yellin 1984).

By and large, there has been a failure to apply to research on the acquisition of voluntary control over autonomic functions what is known about the acquisition of somatic (e.g., motor) skills. The development of somatic skills, especially complex ones, progresses over many "trials" and requires much time, concentration, and perseverance (one may wish to use different terms in referring to animal subjects), with gains still registering after many months or even years of practice (Fitts 1962; 1964; Deese & Hulse 1967). The need to address such issues in research on the acquisition of voluntary ANS-mediated control has been recognized (Miller 1978; 1982). Thus, from the perspective of learning, one might consider most subjects in autonomic-control experiments to have been at an early, "primitive" stage of learning. The above may also explain the generally poor skill retention following discontinuation of training (e.g., Blanchard, Young, Scott & Haynes 1974; 1977; Colgan 1977). Put in other words, most studies on autonomic learning have failed, albeit unintentionally, to address limits of potential. My own ongoing research is demonstrating behaviorally, (Yellin 1984a;b; 1985) and physiologically (Yellin 1984a; Cohn & Yellin 1984) that, with very extensive training, precise cardiovascular control and modulation, via sympathetic and vagal discharge and withdrawal, is possible to an extent not obviously predictable from the existing database. The training (which did not use instrumental feedback) progressed over hundreds of hours and appeared to follow the general pattern characteristic of the acquisition of somatic (e.g., motor) skills (Fitts 1962; 1964). The acquired complex skill, which includes the ability to synchronize (on command) heartbeat to an external Zeitgeber, is as reliable and constantly present, as is a highly developed somatic skill, and is accompanied by a subjective sense of control. Thus, as exemplified by this and by the performance of Engel's highly trained nonhuman primates, length of training is also a critical dimension in visceral learning.

Finally, I would like to expand on Engel's argument that a review of phylogenetic development of the cardiovascular system lends support to the data-based thesis of visceral learning in vertebrates. I believe it does; however, as I pointed out above, "extrapolations" as to how far such learning may progress can turn out to be erroneous if conclusions are drawn solely on the basis of existing data without recognizing the methodological and conceptual constraints that can limit the range of results (Hughes & Roberts 1985). For example, in discussing the accumulated results from experiments on voluntary control of autonomic functions, Davidson (1980; see quotation above) tentatively interprets such data as indicating that the CNS, even at the human level, is "wired" such that there is "little likelihood of conscious manipulation beyond the range of normal variation, [because] conscious access to these processes might permit them to be manipulated in ways which could be biologically hazardous" (p. 26). In fact, we do not yet know what the limits of potential are for somatic, let alone autonomic, learning. The increasing centralization of command functions in the brains of higher animals (Jerison 1973; 1976), especially at the human level, which enables us to impose new demands on our own CNS, as well as on the CNSs of other animals (e.g., through increasingly sophisticated experimental manipulations), means that, among other things, we can both learn and teach new and increasingly complex ways of utilizing our nervous system. I think that this is strongly exemplified by Engel's highly trained monkeys and, even more so, by my own data (Yellin 1985), which, in fact, document the transformation of the heart into a "somatic" organ.

In conclusion, a few words about research strategies: With the (re)emergence of cognitive psychology (and, especially, cognitive psychophysiology), it may be prudent to investigate both response-learning processes as well as cognitive aspects (Furedy & Riley 1982). With respect to the latter, the emergence of new technologies (e.g., computer-controlled and analysed on-line EEG mapping and positron emission tomography) increases our potential and wherewithal to explore the dynamics of cognitive processing. The use of such methods in the exploration of the acquisition of CNS control over ANS-mediated functions may provide remarkable insights into the way that new functional relationships are forged between various CANS (central-autonomic nervous system) structures.

Conditionality of heart rate responses in healthy subjects and patients with ischemic heart disease

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Data from normal and clinical psychophysiology support Dr. Engel's hypothesis that cardiovascular responses are conditional on functional states. It may be that cardiovascular responses are modulated not only by transient changes of functional state (e.g., physical exercise or mental workload, as discussed in the

target article); but also by more continuous changes of functional state associated with varied levels of training in healthy subjects or impaired circulation in patients with IHD (ischemic heart disease). These factors might influence many basic states and conditioned cardiovascular responses.

We have investigated HR (heart rate) responses in healthy subjects with different levels of physical training (Kepeženas & Žemaitytė 1983; Žemaitytė et al. 1984; 1985) and in IHD patients with different levels of blood flow (Žemaitytė et al. 1984; 1984; 1985; 1985). Both healthy subjects and IHD patients were tested during OT (active orthostasis), physical exercise (by veloergometry), and during night sleep stages. Maximal HR changes during OT, exercise, and night sleep stages were calculated. HR power spectra, obtained with the aid of a Hamming window, and HR variability corresponding to its three main periodic components (high frequency or respiration-related, medium frequency or blood-pressure-related, and low frequency, related to thermoregulation and metabolic processes) were measured. The relative distribution of HR variability between reflexive HR (high and medium frequency) and metabolic (low frequency) control was calculated. A maximal HR response during orthostatic testing based on musculocardiac and baroreflexive components (both signs of diminished parasympathetic control) was used to interpret HR reflexive control.

Healthy subjects were shown to have equivalent distributions of HR variability corresponding to the three main periodic components of the HR power spectrum with a slight preponderance of high frequency. Physical exercise reduces HR variability, especially the high frequency component. In deep sleep stages 3-4 (non-REM sleep) there is a relative prevalence of the high frequency component, whereas in REM sleep the low frequency component prevails. The HR increase during OT is nearly 30% above initial HR frequency.

All the HR responses mentioned above are dependent on the functional state of the subject or patient. HR responses during orthostatic testing are highest in well-trained athletes (about 50% from initial HR frequency), as are sleep stage-evoked HRs. HR responses in athletes are related to high workload capacity and central blood flow (stroke volume, cardiac output). Because of high levels of circulation and autonomic HR control (especially parasympathetic), trained athletes have the best ability to interact with the environment: They can reach the same exercise level using lower HR frequency with shorter periods of restitution compared to nontrained subjects or compared to the same person at his lowest functional state.

IHD patients have reduced HR response during OT, exercise, and nocturnal sleep. Under resting conditions, HR variability is diminished and there is a reduction of HR responses during orthostasis. The more marked reduction of the high frequency component, which causes a prevalence of low frequency components in the HR spectrum of IHD patients, points to a reduction of reflexive HR control, especially in the parasympathetic nervous system. The degree of reduction of HR responses in IHD patients is also associated with their functional state. As compared to normal subjects, in IHD patients at low functional states (because of marked ischemic lesions or congestive heart failure) their HR responses during OT and their relative input of the high frequency component of the HR spectrum are twice as low or still lower. Reduced variability of HR responses in the resting state is also paralleled by an equal reduction of HR responses (frequency and variability) during exercise and sleep stages. Diminished HR responses during testing conditions are accompanied by low workload capacity and low blood flow (stroke volume, cardiac output) and by more frequent cardiac abnormalities during exercise and REM sleep. Thus, IHD patients in low functional states accompanied by reduced HR responses have very limited ability to interact with changing environmental conditions. This may involve a reorientation of cardiovascular responses in these patients (as an adaptation to low basic blood flow) to promote survival under a restricted functional range of conditions.

A comparison of athletes with high levels of training and IHD patients with low levels of cardiovascular function shows a wide range of cardiovascular responses conditional on basic state. There exists a wide range of ability to interact with the environment based on the multiplicity of circulatory factors modulating HR responses. The modification of HR responses by functional state, whether the changes are transient or relatively stable, takes place through modulation of autonomic HR control corresponding to basic blood flow.

In conclusion, cardiovascular responses are conditional and determined by basic functional state. They can be interpreted as integral components of behaviour, as indicators of the organism's ability to interact with the environment.

Author's Response

If it looks like a duck, walks like a duck, and quacks like a duck, it is a duck: Neurally mediated responses of the circulation are behavior

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It is not unexpected that 16 commentaries should yield a spectrum of views that are inconsistent among themselves. Two notable examples are (1) **Brener**'s attributing all acquired cardiovascular adjustments to environmental events to somatomotor- or pulmonary-mediated reflexes, in contrast to **Wurster**'s emphasis on central neural programs; and (2) **Bergel**'s puzzling conclusion that my concepts are "useful but unsurprising," as well as his general judgment that findings from experiments using aversive stimuli are not sufficiently important to justify the experiments, in contrast to the view of just about every other commentator. I might add that Brener's peripheralist arguments derive from his theory of learning (1974), which has largely failed to find support (LaCroix & Gowan 1981; Whitehead, Drescher, Heiman & Blackwell 1977). Furthermore, his notion that all circulatory responses are mediated by reflexes elicited by peripheral receptors is inconsistent with the well-established fact that patterned responses of the circulation are emitted by the central nervous system (**Meehan; Sokolov; Wurster;** Eldridge, Millhorn & Waldrop 1981; Hilton 1975). Even Mitchell and Schmidt (1983), whom Brener cites in support of his peripheralist position, make this point strongly (see Section 4, paragraph 17 of my essay).

In general, the comments seem to fall into two broad categories: (1) additional data, mostly supportive but occasionally not; (2) conceptual issues about the functional organization of the brain.

Additional data: Supplementary findings. Several of the commentators agreed that the circulation met the criteria for behavior, and they offered supplemental data to

support this concept. **Billman**'s studies of normal dogs and animals with experimentally induced myocardial ischemia provide interesting and important examples of adaptability. It is well known that patients with ischemic heart disease respond to cardiovascular challenges such as exercise (Clausen & Trap-Jensen 1976) or the cold pressor test (Mudge, Grossman, Mills, Lesch & Braunwald 1976) with increases in left-ventricular work and in coronary vascular resistance that create an imbalance between coronary oxygen supply and myocardial oxygen demand. Thus, these patients are at risk when confronted with stimuli that normally call for increases in heart rate and blood pressure. It is possible that the responses reported by Billman and Randall (1981) indicate acquired, behaviorally mediated mechanisms that help to blunt such reactivity and thus protect the myocardium from further damage. **Wolf** cites the studies of Elsner, Franklin, Van Citters and Kenney (1966) and Elsner and Gooden (1970) in a similar vein. The redistribution of blood volume during the dive reflex has been studied by a number of investigators (even **Bergel** finds the aversive stimulus of enforced diving interesting). The conservation of O_2 during breath retention elicits a powerful reflex that takes precedence over a number of potentially competing reflexes, including the redistribution of blood volume to exercising muscle.

Corley has carried out a series of studies with the squirrel monkey in an effort to characterize some of the behavioral factors that might contribute to the development or progression of cardiomyopathy. The squirrel monkey is known to emit rather large cardiovascular responses to a variety of environmental challenges. Corley's findings seem to indicate that animals who have learned to perform an act that controls an aversive event are less likely to develop serious cardiomyopathies than are animals who either lack the opportunity or the experience to emit such control. A somewhat similar finding has been reported by Lawler, Botticelli, and Lown (1976). Using the dog model described by Lown, Verrier, and Corbalan (1973) (cited in Section 3, paragraph 8), Lawler et al. showed that the ventricular tachycardia threshold to repetitive cardiac stimulation increases as the animal learns to solve the aversive task. These findings are further evidence that cardiovascular adjustments to so-called stressors are really behaviors that become functionally effective with experience.

Meehan has reviewed a number of lines of evidence to support the notion that the responses of the circulation are behavior. He also reports evidence that a variety of circulatory responses can vary significantly as a function of the circadian period (see also Engel 1986) and notes further that these variations in cardiovascular reactivity are modulated by other state-dependent variables, namely, adrenal hormones. The issue of state dependency is also raised by others.

Žemaitytė discusses what he calls the "functional state" of the circulation at the time of challenge. I certainly agree that this is an important quantitative consideration in the assessment of the degree of adaptability of the circulation. Lang, Troyer, Twentyman, and Gatchel (1975) have also reported that state may be a factor in the acquisition of proactive control of heart rate. It is important to recognize that quantitative distinctions exist, since the presence of such determinants provides an additional measure of the sensitivity of physiological control mechanisms.

Yellin also raises the question of basic functional state; however, his concern is not with the cardiovascular state but with the state of the nervous system. In particular, he raises the issue of degree of training in relation to precision of control. I certainly agree that degree of training is an important variable, and we have shown in our monkeys that trained animals emit cardiovascular and somatomotor responses late in training that are quite different from those seen early in training. In particular, many of the somatomotor responses present during the acquisition of heart rate control are no longer present in the well-trained animal (Engel 1974; Engel, Gottlieb & Hayhurst 1976).

Degree of training is especially important in clinical applications. However, just as in the case of **Žemaitytė**'s findings, its main import is quantitative rather than qualitative. It is not clear to me why **Yellin** believes his data provide better examples than do mine or those of Harris and his colleagues (Harris, Gilliam, Findley & Brady 1973; Harris & Turkkan 1981a; Harris & Turkkan 1981b; Harris & Turkkan 1982). Yellin has apparently trained himself to emit rather precisely timed heart beats in synchrony with a metronome beating at various fixed rates. While I agree that his data are impressive, they are limited because they reflect a single individual who may have unique characteristics. I find data from the animal laboratory much more interesting for several reasons: (1) They rule out a host of superfluous interpretations of mechanism, which are usually based on man's capacity to verbalize. (2) They offer far greater opportunity for controlled studies. (3) They provide experimental models, which increase one's opportunity to identify and characterize underlying mechanisms.

Professor **Sokolov** is well known for his extensive research on the nature of innate programs of cardiovascular response and for his research on the extent to which these innate programs can be modified by experience. In his comments he notes particularly his observations on the habituation of the "orienting reflex" and the development – through associative conditioning – of the "defensive reflex." Thus, his work identifies and characterizes a critical bridge between the findings on state dependency (**Meehan, Žemaitytė**) and the development of new, idiosyncratic states resulting from experience (**Yellin**).

The major conclusions from these commentaries are that: (1) Integration of multiple response systems is essential in a functioning organism since any complex act is likely to involve behaviors from one response system that are incompatible with behaviors in another system. (2) Functional behavior will always entail a combination of neural programs (**Wurster**), reflexes (**Del Bo & Zanchetti; Natelson**) and peripheral feedback (**Brener**). (3) The neural program must be plastic and must be determined by an innate program that can be modified on the basis of the antecedents and consequences of the act, that is, on the basis of experience.

Negative evidence, negative arguments. In this section I will address some of the data presented by **Brener** and some of the criticisms raised by **Brener, Roberts, Bergel,**

Del Bo & Zanchetti and **Natelson.** Before doing so, I wish to emphasize two general principles. The first is that negative evidence never nullifies positive findings. Thus, the failure of one or another group of investigators to find a mechanism does not vitiate the findings of others. The second principle is that evidence for one mechanism does not preclude the existence of other mechanisms. This is especially relevant to the circulation and is fundamental to my basic thesis that the behavior of the circulation is multiply determined. In particular, I want to reaffirm my conclusion that cardiovascular responses are reflexes, that the stimuli which elicit these reflexes can be acquired as well as innate, and that the responses can be both emitted to obtain environmental consequences and elicited in response to acquired stimuli. In short, circulatory responses are reactive and proactive.

Brener argues on the basis of two of his own experiments and a partial analysis of one of our studies "that much of the variance in cardiovascular performance attributed to operant conditioning procedures may be understood in terms of the effects of these procedures on striate muscular and respiratory activities." It is not possible to deal in any straightforward way with some of the ambiguity in his statement. I will, therefore, address two issues that seem to be at the heart of his thesis and let the reader decide the matter for himself. First, I will point out that whereas the circulation does support skeletal muscular activity, it does other things as well; second, I will review briefly some of Brener's data and offer some additional data from my laboratory.

It is clear that afferent signals from working muscles provide important feedback information to the brain, which integrates muscle activity with cardiovascular and pulmonary action (Alam & Smirk 1937; Freund, Hobbs & Rowell 1978; Lind, McNicol, Bruce, MacDonald & Donald 1968; McCloskey & Mitchell 1972; Rowell, Hermansen & Blackmon 1976; Saltin, Sjogaard, Gaffney & Rowell 1981). However, it is also clear that the central nervous system is capable of organizing and emitting integrated exercise responses in the absence of such feedback (Eldridge, Millhorn & Waldrop 1981; Goodwin, McCloskey & Mitchell 1972; Hobbs 1982; Johansson 1895; Krogh & Lindhard 1913; Petro, Hollander & Bouman 1970). There are also very important cardiovascular adjustments to the environment that are not at all related to somatomotor or pulmonary function. For example: The circulation provides a major skeletal function in invertebrates such as echinoderms and arachnids – spiders have no extensors and could not move if it were not for their ability to redistribute their blood volume (Prosser 1973); and in penile engorgement of male mammals; and in thermoregulation among homeotherms, which are capable of dissipating heat through the modulation of skin blood flow (Satinoff 1978).

In their 1977 experiment on rats, Brener, Phillips, and Connally reported O_2 consumption of 11 to 19 ml/min using an apparatus that circulated air at the rate of 4 l/min. In their 1980 experiment comparable levels of O_2 consumption were reported using a system that circulated air at 10 l/min. Thus, O_2 consumption values were based on fractions of about 0.3% to 0.5% of the total air volumes. The differences in O_2 consumed were about 0.04% in the 1977 experiments and 0.09% in the 1980 experiments. Although they were studying the relationship between heart rate, activity, and O_2 consumption in conditioning experiments relative to control experiments, it is clear from the data (Brener et al. 1977, Table 1) that the control conditions were unstable. For example, the correlation between heart rate and O_2 consumption was -0.017 during control experiments in subjects which were conditioned to increase heart rate, and the comparable correlation was 0.583 in animals which were conditioned to decrease heart rate. Anyone interested in the problem of cardiovascular and somatomotor interactions should read **Brener**'s papers and decide for himself whether these studies show that all variations in heart rate (that is the only cardiovascular response reported) are necessarily caused by variations in somatomotor or pulmonary activity.

It is very unlikely that any experiment will ever be able to control all the variables that interact with the circulation. This is especially true for experiments with intact subjects. One way to address this problem is to study other conditional cardiac changes for which there is no known relationship between cardiac responses and somatomotor or pulmonary activity. In one such study (Bleecker & Engel 1973a) we showed that patients with atrial fibrillation could learn both to slow and to speed ventricular rate. Because the atrium in these patients is fibrillating, impulses arrive at the atrioventricular (AV) mode at the rate of about 300 to 800 per min and ventricular rate is relatively independent of atrial rate. Thus, in these patients the normal coupling mechanisms between peripheral motor activity and cardiac activity do not exist. As atropine abolished the ability of the subjects to slow or speed ventricular rate whereas isoproterenol, propranolol, and edrophonium had no effect, the results of this study suggest that the patients were modulating vagal tone at the AV node. We have also shown in other studies that patients can learn to increase or decrease the prevalence of ventricular ectopic beats (Weiss & Engel 1971) and of aberrantly conducted beats associated with the Wolff-Parkinson-White syndrome (Bleecker & Engel 1973b). In these arrhythmias as well, there is no clearly established relation between ventricular behavior and peripheral motor activity.

I have tried to show in these few paragraphs that **Brener**'s notion of peripheral determinism is not sufficiently sophisticated physiologically, that the responses of the circulation are multiply determined, and that evidence for the existence of one mechanism – even if it were definitive – would not preclude the existence of other mechanisms. It is also noteworthy that **Wurster**'s discussion of innate programs presents a position that is the diametric opposite of Brener's peripheral determinism. The notion of central neural circulatory regulation has been with us for some time in various forms (Johannson 1895; Krogh & Lindhard 1913). It is now very clear that many of the response patterns that were once believed to have been elicited by peripheral receptors are emitted from the brain. Rowell (1980) has proposed that signals originating in the motor cortex and spinal motor areas activate in parallel both skeletal muscles and cardiovascular efferent systems. Wurster apparently believes (as do I) that the cardiovascular and somatomotor plans are coupled but dissociable.

Roberts's commentary unfortunately seems to be based on numerous misconstruals of fact and unsupported conjectures. Below are some prominent examples, followed by my criticisms.

1. "The motor system (including perceptual processing) is the system by which organisms interact with an environment whose demands and particular features are unique to each member of the species." If one recognizes that the autonomic nervous system is also a motor system, then this is one of the main points of my target article (except for the use of cognitive formulations, which I address below). If **Roberts** wishes to argue that the autonomic nervous system is not a motor system, or that the organizational principles of visceromotor and somatomotor responses are more than what is inherent in their anatomical and physiological structures, then he must provide evidence to support these assertions.

2. "Because the [somato]motor system is specialized for dealing with organism-environment interactions, we would expect this system to be used to solve the problem posed by Engel's operant contingencies." What does **Roberts** mean by "specialized," and what is the evidence that visceromotor systems lack this specialization? (How does Roberts classify O_2 and CO_2 receptors or thermal receptors?)

3. "Unlike the [somato]motor system, the cardiovascular system operates in a milieu that is highly similar for all members of the species." What is the evidence for this? There are certainly enormous differences in the cardiovascular milieus of members of the same species that are: (a) at sea level or submerged in a dive hundreds of feet below sea level; (b) at sea level or on mountaintops high above sea level; (c) in frigid, tropical or temperate climates; (d) at rest or exercising. All these differences can be permuted among one another to yield an extraordinary range of milieus that mammals encounter repeatedly.

4. "[T]he cardiovascular responses required to maintain the internal milieu appear similar enough across situations and conspecifics to diminish the necessity to learn about these responses from a monitoring of their consequences." What does **Roberts** mean by "similar enough" and "diminish the necessity?" One need only consider the enormous range of pH and O_2 concentrations that occur in mixed venous blood. The variance of these basic substances in the venous blood of a single individual in one day is undoubtedly much greater than the variance of these same substances in the air he breathes. If one now factors in the many kinds of stimuli that can affect circulatory responses, the assertion appears difficult to support.

Roberts also raises a number of questions about our studies of cardiac conditioning during exercise (Talan & Engel, in press). (1) He suggests that there are possible differences in patterns of somatomotor behavior but never specifies what these differences might be, nor does he offer evidence that they could account for our results. (2) At one point he mentions the possibility of "sympathetic arousal" during the exercise-only sessions, and elsewhere he wonders about increased sympathetic drive during the combined sessions. Once again, one must ask: What is the evidence that could account for our findings, especially the data indicating that increased sympathetic drive is associated with lower heart rates and equivalent blood pressures? (3) Finally, Roberts raises a number of procedural questions to which I provide the following answers: For all three animals studied, baseline levels were similar between the two conditions; the conditions were counterbalanced within and across days; there were no cues during the baseline periods (nor were there any in the Ainslie & Engel 1974 study); as Figure 5 clearly shows, there were no differences in O_2 consumption between the conditions.

Bergel raises the question of whether the findings from experiments using aversive stimuli justify the use of such stimuli. Actually, this is two questions: (1) Why do investigators use aversive stimuli? (2) Do the results justify their use? There are two reasons for using aversive stimuli. The first is a clinical interest in aversive events; the second is the relevance of aversive stimuli to basic scientific issues. The clinical interest in aversive stimuli derives from the universally held view that aversive stimuli are potentially harmful. If I limit my remarks to the circulation, then the clinical significance of aversive stimuli derives from clinical experience and experimental observation that aversive stimuli are associated with an increased risk of sudden death in subjects with valvular or myocardial disease and excessive rises of blood pressure in subjects with hypertensive disease (e.g., Herd 1984; Verrier & Lown 1984).

Scientists who are interested in these clinical problems (e.g., Corley, Lown, Verrier & Corbalan 1973; Anderson, Kearns & Better 1983) have developed and studied animal models to demonstrate the potency of aversive stimuli and their implications for the human condition, and because they hope to use these models to test a variety of therapeutic agents. I believe that most people recognize the value of such research programs and that further detailed defense of them is unnecessary. We have discovered that when monkeys are taught to cope with an aversive stimulus such as tail shock by slowing their heart rates, they can do so readily. (Incidentally, we have also recently shown that monkeys can learn to control their systolic pressures; Bardos, Talan & Engel, in preparation.) This finding suggests that aversive events are not immutable (and that this aspect of the circulation as behavior might be useful and even surprising).

There are several basic scientific reasons why aversive stimuli are used. One is that there is at least one innate program (**Wurster**), the "defensive reflex" (**Sokolov**; Hilton 1975) that depends for its expression on the use of aversive stimuli in intact animals. I thought our experiments with the exercising monkey (Talan & Engel, in press) would be of some interest to physiologists because it provides an experimental model for the study of an obscure physiological concept that has several euphemisms (cortical irradiation, central command) but little substantive data.

Another reason for using aversive stimuli is to produce reliable behavior efficiently. Reinforcers such as food have been used in some studies; however, these have introduced a host of interpretational complications resulting from the interaction between prior state (food deprivation) and concomitant performance (consumatory behavior) on the cardiovascular responses of interest. An even more serious problem is that rewards as contingent

stimuli have been found to produce greater variability in behavior than aversive stimuli. Thus, one is likely to need more animals when one uses rewards. Whereas I have emphasized efficiency as a criterion, there are some scientists who equate the number of subjects used with humanitarianism, and who would argue that those experiments using the fewest animals are the most humane.

The question of justifying the use of animals in research is an interesting one. Despite the large literature based on religious or ethical teachings, it has never been possible to achieve unanimity on when an end justifies a means. As a result, mankind in general, and scientists in particular, have taken a conservative position based primarily on the view of the majority. If the sample of commentaries on my essay are any criterion, **Bergel** seems to stand alone.

Del Bo & Zanchetti's and **Natelson**'s desires to preserve the reflex put them somewhere between **Brener**'s naive peripheralism and **Wurster**'s centralism. Each seems to have created his own straw man. Del Bo & Zanchetti interpret my essay to imply that "the central nervous system, acting in the context of information accumulated at a certain time, is solely responsible for producing not only a given behavior but also its accompanying cardiovascular changes." Natelson opposes throwing out "the baby with the bath water." He wishes "to argue for the primacy of the reflex and for the need to fill in many blanks before we can be sure that cardiovascular 'behavior' is identical to skeletal motor 'behavior.'" There are two things wrong with Del Bo & Zanchetti's attribution: First, I never proposed that the CNS is solely responsible for producing every behavior; and, second, I believe that the "accompanying cardiovascular changes" are themselves behavior and are sometimes leading rather than accompanying.

I do not know what **Natelson** means by primacy, nor do I know which is the baby and which is the bath water. Besides, throwing either out seems unnecessary! I do believe, however, that cardiovascular and skeletal motor behaviors are identical in the tripartite sense in which I defined behavior. I made my views on reflexes clear in the last sentence of my essay. They are not banal; however, one needs to consider them in context.

I believe **Del Bo & Zanchetti**'s view that "both actors, the central command and the reflex feedback, are always on stage" is precisely my position. The main difference is that in their drama they wish to emphasize the reflex feedback, whereas I have emphasized the central command. But both actors are indeed always on stage. I do suspect, however, that when they have "worked out" their "proposition," they will find that in the intact subject who is interacting with his environment, central command is the star and the reflex feedback plays a supporting role.

Natelson emphasizes the fact that under some experimental conditions, classically conditioned cardiac reflexes do not extinguish. First of all, there are many experimental conditions under which somatomotor responses do not extinguish (Guthrie & Horton 1946; Solomon, Kamin & Wynne 1953). There are also many anecdotal examples of ritualistic motor behaviors e.g., repetitive acts performed by athletes, such as the number of times a baseball player taps home base before he takes his stance, or how many times a golfer waggles his club before striking the ball). Second, there are many experimental conditions under which cardiovascular responses do extinguish. In our experiments, if the tail shock is disconnected, even a well-trained animal will extinguish.

Conceptual issues. At one time I believed that cognitive theories of behavior that used concepts such as perception or mind were useful and necessary, because they provided descriptive mechanisms that accounted for the range of complex human behaviors. My dissatisfaction with these notions has evolved since the early 1960s. First, I found the mind–body dualism disconcerting and biologically unreasonable, since cognitive models depend so heavily on verbal behavior (**Wolf**). It seems clear to me that any model of animal function that is species-specific is scientifically inadequate.

Over the last 25 years, two further problems with cognitive models have made me turn to straightforward behavioristic models: One is that cognitive models of brain function reintroduce the untenable concept of the homunculus; the second is that cognitive models of clinical intervention are inadequate, and perhaps even potentially harmful. Under these circumstances, it was surprising to read that **Jennings** believes that I have rediscovered cognition! I assure him, one does not need to rediscover a plague, as one is forever surrounded by its effects.

Cognitive models of brain function draw heavily on the notion that brain organization and function can be modelled after modern computer operation (**Jennings**; **Roitblat**). As someone who has designed and used computers for 30 years now, I believe I have some understanding of the strengths and limitations of such systems. As is well known, when Von Neumann developed his model of a computing machine, he did so by speculating about how the brain worked; he then patterned his design accordingly. Although it is ironic that this hypothesis should have become so generally accepted as truth by so many scientists, it is not a sufficient criticism of the validity of the cognitive model, since Von Neumann's hypothesis could be correct. His computer design has several components that all modern computers retain. First, there is a central processor that includes: (1) an accumulator, which is a register where all operations occur; (2) an instruction register, which contains the rules that determine the accumulator operation; (3) a (possibly recursive) program counter that keeps track of the sequence of operations; (4) various other registers, which permit real and virtual memory stores to be addressed either directly or indirectly. In addition to the central processing unit, all computers have a number of ancillary devices, including input and output devices and immediate and remote memory stores.

The main problem for me in applying this model to the brain has always been that this hardware system is passive; its function depends upon the preexistence of a program. Since every program I have ever seen was developed by a programmer, that means that this model of the brain needs a programmer; even computers that "learn" need to be programmed to do that. The cognitive programmer is the modern day homunculus! The software package needed to manage the cognitive oper-

ating system is very sophisticated indeed. Input information needs to be encoded with labels so constructed that they will be able to anticipate future applications, which have never been implemented because the encoded information needs to be selectively and reliably retrieved. Only a homunculus (possibly operating in collaboration with Maxwell's demon) could do the job.

My behavioristic model of the brain lacks the sentience of the cognitive version. It is predicated on the neurophysiological observation that there are genetically determined motor plans (**Wurster**'s innate programs). These plans can be modified in two ways:

(1) The receiving areas that release the plan can be penetrated by axons that will provide input from a variety of receptors. These inputs are determined by two factors: (a) growth (i.e., genetic preprogramming and (b) development (i.e., experience operating in a milieu defined by the anatomical and physical constraints of brain structure and function). There is no homunculus to encode anything; there are merely connections, some of which exist and some of which develop.

(2) The motor areas that express the plan impinge on effectors and on other innate programs. These efferent projections also evolve through growth and development, and, like all effectors, they can be excitatory or inhibitory. I emphasize (for **Brener**) that motor plans are emitted. Experience (**Yellin**'s "training") determines the probability of occurrence of various motor plans through several mechanisms:

1. Antecedent events (contextual stimuli) elicit particular responses. In my essay I reviewed at some length the evidence that not only can these stimuli elicit responses innately, but they can also acquire their eliciting properties through experience, i.e., through their consequences. Some of the commentators offered additional evidence.

2. Physiological states (**Meehan**'s catecholamine and steroid levels, determined in part by diurnal rhythms – see also Engel 1986; brain stem oscillators – e.g., Gebber, Barman, Morrison & Ardell 1982) contribute to the likelihood that a particular motor plan will be emitted.

3. Stimuli that occur as a consequence of particular behaviors will modify the likelihood that those behaviors recur.

Two mechanisms by which these consequent effects might mediate behavior are by modifying physiological states so that subsequent behaviors occur in a modified context; and by directly changing central hormonal states that modulate the development of neural connections (e.g., endorphins might facilitate the development of excitatory synapses).

This model – which is admittedly speculative – requires no homunculus who "recognizes" information, "retrieves" memories and "compares" (Brener 1974) the information with an engram, then "loads" a program that determines the consequent behavior. Behavior happens because it is in part innately determined and in part acquired through experience. Behavior can be reactive because it can be elicited by environmental events whose properties are innately determined (e.g., thermal stimuli), and it can be elicited by environmental stimuli whose properties are acquired through experience. Behavior can also be emitted because the physiological states increase the likelihood of one pattern of response over another; or it can be emitted because the physiological state is altered by the behavior itself.

Finally, it should be noted that this model does not attribute purpose to behavior. Behavior is not emitted because it is seen to be good by a sentient homunculus. Rather, it is emitted because antecedent and consequent events, historically and contemporarily – qua, experience – have modified the motor plans so as to change their relative probabilities of occurrence. Before leaving this section I want to point out that **Wurster**'s proposal that innate programs can be equated with behavior is valid; but what makes behavior biologically significant (in the sense that it facilitates natural selection) is that these innate programs are modifiable. This is not just a semantic argument as to the nature of an innate program; I am suggesting that the various programs that have been identified as controlling circulatory effects are really templates that adapt with experience.

I indicated earlier that the second reason I reject cognitive models of behavior is that I have found them clinically unsatisfying. Although cognitive models of therapy have evolved considerably over the last 25 years, they still tend to have undesirable features. It is wholly outside the scope of this paper to review all these issues; however, I suggest that the interested reader look at my presidential address to the American Psychosomatic Society (Engel, in preparation) for my views on some of these questions. He could also look at some of the clinical results my colleagues and I have obtained using behavioristic models and techniques (Baile & Engel 1978; Bleecker & Engel 1974; Burgio, Whitehead & Engel 1985; Engel, Glasgow & Gaarder 1983; Engel, Nikoomanesh & Schuster 1974; Whitehead, Burgio & Engel 1985). I particularly suggest that the interested reader compare the cost-effectiveness of our treatment strategies with some of the therapeutic models used by cognitively oriented therapists.

Roitblat presents an interesting analysis of the relationship of my essay to cognitive models of behavior. Since I have already listed my objections to cognitive models, I will not repeat them. However, I do want to note two logical problems Roitblat's commentary raises. One is that some theorists have found it necessary to propose a dichotomy between cognitive and noncognitive behaviors, and the second is the possibility that findings such as mine "penetrate" the boundary between these two behaviors.

First, it is very difficult for me to imagine that behavior can be dichotomized. If one stays within the cognitive framework, and if one believes that behavior is dichotomous, one must also believe that the encoder knows the difference between behaviors. How then does one deal with the expression of both forms of behavior at the same time? Does the "retriever" know the purpose for which the engram has been retrieved? Are there separate retrievers? Do they talk to one another? Does one take precedence over the other, and if so, what are the rules the homunculus follows?

The question of the penetration of the boundary is very serious theoretically. Not only does it raise the possibility that the boundary has been misplaced, it also raises the possibility that the boundary does not exist. If

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the boundary does not exist, then perhaps a proper analysis would reveal that all behaviors are noncognitive. (Perhaps, one day **Jennings** will even discover behavior!)

The last conceptual issue I shall consider is that raised by **Sandman.** He addresses the question of the cognitive significance of feedback from cardiovascular responses to the brain and speculates on the role this feedback has on consciousness. As Sandman himself notes, his discussion parallels mine but is unrelated to my concerns. Although I would not use such terms as consciousness, I have no substantive quarrel with Sandman's analysis. Certainly, in a deterministic world such as the one I have drawn, afferent signals from whatever source must contribute to the final acts.

Reprise. I have tried in my essay and in my responses to the commentators to make the case that neurally mediated responses of the circulation meet the criteria for behavior because they can be elicited and because they can be emitted. Nowhere have I rejected the notion that many of the responses of the circulation are reflexes. However, I did state that I thought that when an animal interacts with its environment, many reflexes operate simultaneously; that some of these are incompatible with others; and that performance is always an integrated action. I was a bit surprised by the concern that **Natelson** expressed for the viability of the reflex. He entitled his commentary "The reflex remains." I certainly did not send it away. I also agree with **Wurster** that cardiovascular responses are determined, in part, by innate programs. However, I have tried to make the case that these programs are templates for development and not merely superordinate reflexes.

I share the concern that many psychologists have for people, and, as I have noted, I do see and treat patients. However, I do not believe there can be a science of man based on a discontinuity among orders. Although I recognize that cognitive theorists have progressed from the stage of development when they ignored nonhuman species, I still find their models too anthropocentric, and the dualism implicit in some of their dichotomies is an anathema to me. I hope that **Roitblat** will reflect on the implications of penetrability.

Finally, I disagree with **Wolf** about the clinical importance of verbal behavior; in particular, I believe the verbal "communication of thoughts and emotions" can be confounding, since verbal reports of behavior often are unreliable and inconsistent with direct observations. As a scientist, I am far more limited in my abilities to study people than I am to study animals. As Wolf knows well, the greatest progress in clinical medicine has come from an understanding of basic mechanisms. That will be just as true for behavioral mechanisms as it is for any other biological mechanism.

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